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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09   CA/CAplus records now contain indexing from 1907 to the
                   present
 NEWS  4  DEC 08   INPADOC: Legal Status data reloaded
 NEWS  5  SEP 29   DISSABS now available on STN
 NEWS  6  OCT 10   PCTFULL: Two new display fields added
 NEWS  7  OCT 21   BIOSIS file reloaded and enhanced
 NEWS  8  OCT 28   BIOSIS file segment of TOXCENTER reloaded and enhanced
 NEWS  9  NOV 24   MSDS-CCOHS file reloaded
 NEWS 10  DEC 08   CABA reloaded with left truncation
 NEWS 11  DEC 08   IMS file names changed
 NEWS 12  DEC 09   Experimental property data collected by CAS now available
                   in REGISTRY
 NEWS 13  DEC 09   STN Entry Date available for display in REGISTRY and CA/CAplus
 NEWS 14  DEC 17   DGENE: Two new display fields added
 NEWS 15  DEC 18   BIOTECHNO no longer updated
 NEWS 16  DEC 19   CROPU no longer updated; subscriber discount no longer
                   available
 NEWS 17  DEC 22   Additional INPI reactions and pre-1907 documents added to CAS
                   databases
 NEWS 18  DEC 22   IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
 NEWS 19  DEC 22   ABI-INFORM now available on STN

 NEWS EXPRESS  DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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FILE 'HOME' ENTERED AT 15:30:24 ON 22 JAN 2004

=> FIL REGISTRY
COST IN U.S. DOLLARS                          SINCE FILE       TOTAL
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                                                        ENTRY     SESSION
FULL ESTIMATED COST                                      0.21        0.21

FILE 'REGISTRY' ENTERED AT 15:30:45 ON 22 JAN 2004
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STRUCTURE FILE UPDATES:   21 JAN 2004  HIGHEST RN 640234-51-1
DICTIONARY FILE UPDATES:  21 JAN 2004  HIGHEST RN 640234-51-1

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s GTKVHMK/SQEP
             1 GTKVHMK/SQEP
         44884 SQL=7
L1           1 GTKVHMK/SQEP
                 (GTKVHMK/SQEP AND SQL=7)

=> s GTKVHMK/SQSP
L2          45 GTKVHMK/SQSP

=> S PGTSGQQPSVGQQ/SQEP
             1 PGTSGQQPSVGQQ/SQEP
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L3           1 PGTSGQQPSVGQQ/SQEP
                 (PGTSGQQPSVGQQ/SQEP AND SQL=13)

=> S PGTSGQQPSVGQQ/SQSP
L4          68 PGTSGQQPSVGQQ/SQSP

=> S PKPSTPPGSS/SQEP
             2 PKPSTPPGSS/SQEP
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L5           2 PKPSTPPGSS/SQEP
                 (PKPSTPPGSS/SQEP AND SQL=10)

=> S PKPSTPPGSS/SQSP
L6          55 PKPSTPPGSS/SQSP

=> S SGGTSGSTSGTGST/SQEP
             1 SGGTSGSTSGTGST/SQEP
         43809 SQL=14
L7           1 SGGTSGSTSGTGST/SQEP
                 (SGGTSGSTSGTGST/SQEP AND SQL=14)

=> S SGGTSGSTSGTGST/SQSP
L8           1 SGGTSGSTSGTGST/SQSP

=> S AGSSTGSSTGPGSTT/SQEP
             1 AGSSTGSSTGPGSTT/SQEP
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L9           1 AGSSTGSSTGPGSTT/SQEP
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=> S AGSSTGSSTGPGSTT/SQSP
L10          1 AGSSTGSSTGPGSTT/SQSP

=> S GGSGGAP/SQEP
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L11          1 GGSGGAP/SQEP
                 (GGSGGAP/SQEP AND SQL=7)

=> S GGSGGAP/SQSP
L12         61 GGSGGAP/SQSP

=> d hist

     (FILE 'HOME' ENTERED AT 15:30:24 ON 22 JAN 2004)

     FILE 'REGISTRY' ENTERED AT 15:30:45 ON 22 JAN 2004
L1           1 S GTKVHMK/SQEP
L2          45 S GTKVHMK/SQSP
L3           1 S PGTSGQQPSVGQQ/SQEP
L4          68 S PGTSGQQPSVGQQ/SQSP
L5           2 S PKPSTPPGSS/SQEP
L6          55 S PKPSTPPGSS/SQSP
L7           1 S SGGTSGSTSGTGST/SQEP
L8           1 S SGGTSGSTSGTGST/SQSP
L9           1 S AGSSTGSSTGPGSTT/SQEP
L10          1 S AGSSTGSSTGPGSTT/SQSP
L11          1 S GGSGGAP/SQEP
L12         61 S GGSGGAP/SQSP

=> FIL CAPLUS BIOSIS MEDLINE PCTFULL USPATFULL EUROPATFULL JAPIO SCISEARCH EMBASE
USPAT2 EUROPATFULL
COST IN U.S. DOLLARS                                SINCE FILE    TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                  207.42     207.63

FILE 'CAPLUS' ENTERED AT 15:43:13 ON 22 JAN 2004
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FILE 'USPAT2' ENTERED AT 15:43:13 ON 22 JAN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> s apolipoprotein
L13     137818 APOLIPOPROTEIN

=> s l1 or l2 or l3 or l4 or l5 or l6 or l7 or l8 or l9 or l10 or l11 or l12
'SQEP' IS NOT A VALID FIELD CODE
'SQSP' IS NOT A VALID FIELD CODE
   5 FILES SEARCHED...
'SQEP' IS NOT A VALID FIELD CODE
'SQSP' IS NOT A VALID FIELD CODE
'SQEP' IS NOT A VALID FIELD CODE
'SQSP' IS NOT A VALID FIELD CODE
'SQEP' IS NOT A VALID FIELD CODE
'SQSP' IS NOT A VALID FIELD CODE
L14        134 L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR
               L11 OR L12

=> s l13 and l14
L15         22 L13 AND L14

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16          22 DUP REM L15 (0 DUPLICATES REMOVED)

=> d l16 1-22 bib hit

L16  ANSWER 1 OF 22  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:913280  CAPLUS
DN   139:379453
TI   Genes showing altered patterns of expression in multiple sclerosis and
     their diagnostic and therapeutic uses
IN   Dangond, Fernando; Hwang, Daehee
PA   Brigham and Women's Hospital, Inc., USA
SO   PCT Int. Appl., 148 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     --------------    ----  --------      ---------------  --------
PI   WO 2003095618     A2    20031120      WO 2003-US14462  20030507
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-379284P   P     20020509
     US 2003-430762    A1    20030506
IT   479329-25-4, Zinc finger protein (human gene ZNF141)   479329-27-6, Rieske
     Fe-S protein (human gene UQCRFS1)   479329-66-3, AP-3 complex beta3A
     subunit (human)   479329-82-3   479329-83-4, Protein (human gene ZAKI-4)
     479329-84-5   479329-88-9   479329-90-3   479329-91-4   479329-94-7,
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Osteonidogen (human) 479329-97-0 479330-07-9 479330-08-0 479330-10-4 479330-12-6 479330-16-0 479330-39-7, Selenium donor protein (human gene selD) 479330-43-3 479330-47-7 479330-48-8, N33 protein form 1 (human gene N33) 479330-53-5 479330-56-8 479330-59-1 479330-61-5, RNA-binding protein HuR (human gene HuR) 479330-72-8, Acyl-CoA dehydrogenase (human gene SCAD) 479330-81-9, Protein (human 254-amino acid) 479330-83-1, Protein (human 524-amino acid) 479330-85-3 479331-24-3, Protein (human gene CEA) 479331-25-4, Protein (human gene CP) 479331-30-1, Glucose transporter (human gene GLUT4) 479331-43-6 479474-75-4 479474-86-7, Laminin S B3 chain (human gene LAMB3) 479475-19-9 479475-48-4, Protein (human gene HNL) 479475-59-7 479476-00-1, Glutaredoxin (human gene grx) 479476-04-5 479476-84-1 479476-90-9 479476-92-1, Isopeptidase T (human gene ISOT) 479476-95-4, Pin1 (human cell line HeLa gene PIN1) 479476-96-5, GenBank AAC50737 479477-55-9 479477-59-3 479477-63-9, PACAP receptor (human) 479477-71-9, Protein (human clone 39H11 gene LLGL) 479477-80-0 479478-05-2, Oviductal glycoprotein (human) 479478-30-3, Metallothionein IV (human gene MTIV) 479478-37-0, Protein (human 401-amino acid) 479478-40-5 479478-43-8, Protein (human 514-amino acid) 479478-45-0 479478-47-2, Protein (human 511-amino acid) 479478-56-3, Protein (human gene IGF1R) 479478-62-1, Renin (human gene REN) 479478-63-2, Mannose receptor (human gene MRC1) 479660-47-4 479660-77-0 479660-79-2 **479660-93-0**, Fibronectin precursor (human) 479660-94-1, Protein (human 937-amino acid) 479796-75-3, Cysteine dioxygenase type 1 (human) 479797-48-3 479800-10-7 479800-11-8 479800-22-1 479800-32-3, Cardiotrophin-1 (human gene CTF1) 479800-41-4 479840-33-0, Hemochromatosis protein (human) 479850-86-7, LERK-3 (human gene EPLG3) 479854-95-0 479857-37-9 479864-78-3 479864-79-4 479872-00-9, CLN3 protein (human clone 2-3 gene CLN3) 479911-76-7 479911-77-8 479954-16-0 479962-50-0 479966-85-3, Protein (human gene -14) 479968-02-0, GenBank CAA51391 479974-05-5 479974-06-6 479976-19-7 480000-04-2, A2a adenosine receptor (human) 480087-26-1 480101-37-9, FUSE binding protein (human) 480110-95-0, Protein WSL-1R (human gene wsl-1) 480110-96-1, Protein WSL-S1 (human gene wsl-1) 480110-97-2, Protein WSL-S2 (human gene wsl-1) 480111-35-1, ZFX product, isoform 2 (human gene ZFX) 480111-37-3 480111-73-7 480112-14-9 480121-88-8, Protein (human 284-amino acid) 480122-13-2 480122-91-6, Protein (human 135-amino acid) 480123-18-0 480123-44-2, Protein (human clone 1 318-amino acid) 480123-70-4, Synaptophysin (human) 480124-06-9, Protein (human 192-amino acid) 480125-05-1, SnRNP B protein (human gene snRNP B) 480125-15-3, GenBank CAA37171 480125-16-4, GenBank CAA37170 480125-27-7 480125-75-5 480126-30-5 480126-47-4 **480126-70-3** 480126-88-3 480126-97-4 480127-17-1 480127-33-1 480127-34-2, Rab 13 (human gene rab 13) 480127-81-9, Protein (human clone MK5 496-amino acid) 480128-07-2 480128-11-8, Ret fused gene (human gene RFG) 480128-29-8, Phosphorylase kinase (human gene PHKG1) 480128-30-1 480128-31-2, R kappa B (human cell line HUT-78) 480128-32-3, Gp50/Trop-2 (human gene TROP-2) 480128-44-7 480128-46-9 480128-47-0 480128-60-7 480129-10-0 480129-20-2, RagB (human) 480129-69-9, RING finger protein (human gene RFB30) 480130-04-9 480130-10-7, ROX protein (human gene rox) 480130-12-9 480130-29-8 480131-06-4 480131-14-4, Taurine transporter (human) 480132-32-9, PQ-rich protein (human) 480132-55-6, Metalloproteinase (human clone 15-1) 480132-60-3, P40 (human cell line Jurkat gene p40) 480138-80-5, **Apolipoprotein** C-II (human gene APOC2) 480287-38-5, GenBank AAB30847 480287-67-0 480288-52-6, Calpastatin (human gene CAST) 480288-53-7 480288-54-8 480288-76-4, P54/58N (human gene MaTu MN) 480288-84-4, Protein (human 403-amino acid) 480532-53-4 480532-54-5 480532-55-6 480532-98-7 480533-78-6, GenBank AAD14281 480534-07-4, GenBank AAD14320 480567-37-1 480572-55-2, CD40 antigen (human) 480580-12-9, G18 (human) 480580-13-0, Homeobox PBX2 gene (human gene HBX2) 480580-14-1 480580-15-2, G16 (human) 480580-16-3, LPAAT (human) 480580-17-4, NG3 (human) 480580-18-5, PPT2 (human) 480580-19-6, NG5 (human) 480580-24-3 480580-27-6, P41-Arc (human gene ARC41) 480580-30-1,

P20-Arc (human gene ARC20) 480593-54-2 480593-78-0 480595-08-2 480595-98-0 480598-27-4 480606-76-6, PH-20 (human gene SPAM1) 480606-82-4, Con1 (human gene PRB2) 480606-87-9, GenBank AAB36381 480615-84-7 480618-20-0 480618-21-1 480618-30-2, Protein (human 503-amino acid) 480620-83-5 480624-83-7 480627-36-9 480627-37-0 480628-18-0, Protein (human gene a-myb) 480632-36-8 480634-51-3, Aldolase C (human gene ALDOC) 480634-58-0, Aldolase A (human clone lambda A3.) 480637-42-1 480643-07-0 480643-39-8, Protein (human 559-amino acid) 480643-42-3, Protein (human gene EVX1) 480643-82-1 480643-83-2 480644-89-1, Protein (human clone S7 297-amino acid) 480644-91-5 480644-98-2, Catechol O-methyltransferase (human) 480645-04-3 480645-14-5, Protein (human gene brca2) 480645-62-3, Protein (human 403-amino acid) 480645-80-5, Cathepsin O (human clone O7-7) 480647-10-7 480648-61-1, Protein (human clone 641/643 gene hCHML) 480649-16-9, Beta adducin (human clone K11, K3) 480649-20-5 480649-54-5 480650-22-4, Zeta-globin 1 (human clone GG1) 480650-23-5, Alpha-globin 1 (human clone GG1) 480650-24-6, Alpha-globin 2 (human clone GG1) 480650-45-1 480650-58-6 480651-16-9, BGP (human) 480651-36-3 480651-38-5 480651-66-9, Casein kinase II subunit beta (human) 480651-80-7 480652-31-1 480652-33-3, Cystain S (human) 480652-44-6 480653-32-5, Elongation factor 2 (human) 480653-35-8, Protein (human gene c-fes) 480653-44-9, Protein (human leukocyte 161-amino acid) 480653-76-7 480653-79-0 480653-86-9 480654-29-3 480654-48-6, Protein (human gene ENA-78) 480654-54-4, Protein (human 505-amino acid) 480654-55-5, Protein (human 241-amino acid) 480655-74-1, Protein (human 1537-amino acid) 480656-86-8, Protein (human gene L23-related gene) 480656-98-2 480656-99-3 480659-47-0 480660-09-1 480661-25-4 480661-42-5 480661-53-8 480661-92-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes showing altered patterns of expression in multiple sclerosis and their diagnostic and therapeutic uses)

L16 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:942764 CAPLUS
DN 140:3792
TI Genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics
IN Nevins, Joseph; West, Mike; Goldschmidt, Pascal
PA Duke University, USA
SO PCT Int. Appl., 408 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003091391	A2	20031106	WO 2002-XA38221	20021112
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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PRAI US 2002-374547P P 20020423
US 2002-420784P P 20021024
US 2002-421043P P 20021025
US 2002-424680P P 20021108
WO 2002-US38221 A 20021112
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RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics)

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RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics)

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392027-39-3 392027-43-9 392027-44-0 392027-46-2 392027-48-4
392027-50-8 392027-53-1 392027-55-3, GenBank AB007900 392027-62-2, GenBank AB007922 392027-71-3 392027-73-5, GenBank AB007947

392027-80-4 392029-52-6, DNA (human clone 23851 cDNA) 392029-64-0 392029-83-3, DNA (human clone hg001041 gene KIAA0446) 392029-84-4 392029-89-9 392029-90-2 392029-95-7 392029-96-8, DNA (human clone HH1176 cDNA) 392029-97-9 392029-99-1, DNA (human clone HG0144 cDNA) 392031-45-7 392031-50-4 392031-98-0 392032-35-8 392034-29-6, DNA (human clone ntcon5 contig cDNA) 392034-33-2, DNA (human gene USA-CyP cDNA) 392034-36-5, DNA (human gene CA 12 cDNA) 392036-94-1 392036-96-3, DNA (human protein 4.1-G cDNA) 392037-07-9, DNA (human gene FIBP cDNA) 392037-26-2, DNA (human gene RZF cDNA) 392037-61-5, DNA (human alpha endosulfine cDNA) 392037-63-7 392037-77-3, DNA (human gene nipsnap1 cDNA) 392038-08-3 392038-10-7 392038-36-7, DNA (human clone 23923 cDNA) 392038-46-9 392039-02-0 392039-05-3 392039-33-7, GenBank AF043472 392039-63-3 392039-73-5 392039-76-8 392042-24-9, DNA (human NRAMP2 cDNA) 392043-62-8 392043-70-8 392043-79-7 392043-81-1 392043-84-4, DNA (human ZIP-kinase cDNA) 392044-15-4, DNA (human gene BUB3 cDNA) 392045-08-8 392045-17-9, DNA (human gene MMS2 cDNA) 392046-52-5 392046-72-9, DNA (human gene SMARCA5 cDNA) 392047-22-2 392047-89-1, DNA (human cell line HepG2 p115 cDNA) 392048-71-4, DNA (human gene UBE2G2 cDNA) 392048-74-7 392048-83-8 392048-90-7, GenBank AF055029 392049-31-9 392049-32-0 392049-35-3 392049-62-6, DNA (human gene CTNS cDNA) 392049-78-4, DNA (human perilipin cDNA) 392049-83-1 392049-93-3 392050-05-4 392050-13-4 392050-21-4 392050-26-9 392050-29-2 392050-32-7 392050-38-3 392050-39-4, DNA (human gene EDF-1 cDNA) 392050-48-5, DNA (human gene GSTA4 cDNA) 392051-48-8, DNA (human gene HCAP cDNA) 392051-74-0 392051-93-3 392052-03-8, GenBank AF055872 392052-34-5, DNA (human gene UGDH cDNA) 392052-44-7, DNA (human clone RP3-347H13) 392052-61-8 392052-70-9, GenBank AF036927 392052-71-0 392053-57-5 392054-53-4 392054-54-5, DNA (human gene RAMP3 cDNA) 392054-88-5, DNA (human VESPR gene cDNA plus flanks) 392055-40-2, DNA (human gene G2AD cDNA) 392055-51-5, DNA (human gene ADSL cDNA) 392057-11-3, GenBank U75744 392057-54-4, DNA (human gene BCNT cDNA) 392057-69-1 392057-71-5 392057-79-3 392058-06-9 392058-07-0 392058-09-2 392058-11-6 392058-20-7, DNA (human ES/130 cDNA) 392058-30-9 392058-64-9, DNA (human gene NRPB cDNA) 392058-73-0, DNA (human protein associated with Myc) 392058-75-2, DNA (human gene tom1 cDNA) 392058-86-5 392058-87-6 392058-91-2 392058-92-3 392058-95-6 392058-98-9 392058-99-0 392059-00-6 392059-04-0 392059-09-5 392059-10-8 392059-13-1 392059-14-2 392059-16-4 392059-19-7 392059-24-4 392059-27-7 392059-49-3 392059-62-0 392059-72-2 392059-79-9, DNA (human histone macroH2A1.2 cDNA) 392059-90-4, DNA (human p18 protein cDNA) 392059-94-8 392060-37-6 392060-41-2 392060-59-2 392061-48-2 392061-72-2, DNA (human clone RP5-886K2)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics)

L16 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:150445 CAPLUS
DN 138:199935
TI A bifunctional recombinant virus ligand fusion protein containing an antibody binding region and its use for specific cell targeting in gene therapy
IN Li, Yibing
PA Rainbow Therapeutic Company, USA
SO U.S., 24 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6524572	B1	20030225	US 2000-604107	20000626

PRAI US 2000-604107 20000626
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT **Apolipoproteins**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A-I, therapeutic; bifunctional recombinant virus ligand fusion protein contg. an antibody binding region and its use for specific cell targeting in gene therapy)
IT **Apolipoproteins**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C, therapeutic; bifunctional recombinant virus ligand fusion protein contg. an antibody binding region and its use for specific cell targeting in gene therapy)
IT **Apolipoproteins**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E, therapeutic; bifunctional recombinant virus ligand fusion protein contg. an antibody binding region and its use for specific cell targeting in gene therapy)
IT **499802-73-2P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; bifunctional recombinant virus ligand fusion protein contg. an antibody binding region and its use for specific cell targeting in gene therapy)

L16 ANSWER 4 OF 22 USPATFULL on STN
AN 2003:330210 USPATFULL
TI Protein-protein interactions in adipocyte cells (3)
IN Legrain, Pierre, Paris, FRANCE
Whiteside, Simon, Cambridge, UNITED KINGDOM
Mao, Jen-I, Palo Alto, CA, UNITED STATES
Khrebtukova, Irina, San Francisco, CA, UNITED STATES
Luo, Shujun, Berkeley, CA, UNITED STATES
PA Hybrigenics, Paris, FRANCE (non-U.S. corporation)
PI US 2003232421 A1 20031218
AI US 2002-139794 A1 20020506 (10)
PRAI US 2001-288885P 20010504 (60)
DT Utility
FS APPLICATION
LREP LERNER, DAVID, LITTENBERG,, KRUMHOLZ & MENTLIK, 600 SOUTH AVENUE WEST, WESTFIELD, NJ, 07090
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 13515
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0381]
TABLE 2

bait-prey interactions

1. Bait name	2. DNA bait SEQ ID	3. AA bait SEQ ID	4. Prey
Full-length human SPARC	1	2	dbj|AB033073.1|AB033073 Homo sapiens mRNA for KIAA1247 protein, partial cds
Full-length human SPARC	1	2	dbj|AB040964.1|AB040964 Homo sapiens mRNA for KIAA1531 protein, partial cds
Full-length	1	2	dbj|AP001697.1|AP001697 Homo sapiens genomic

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Human HIP2          11      12      gb|AC002073.1|AC002073 Human PAC clone
       RP3-515N1 from 22q11.2-q22, complete sequence [Homo
(full-length)                       sapiens]
Human HIP2          11      12      gb|AC005185.1|AC005185 Homo sapiens Xp22 bins
       169-171 BAC GSHB-383H3 (Genome Systems
(full-length)                       Human BAC Library) complete sequence
Human HIP2          11      12      gb|AC006101.3|AC006101 citb_338_f_24, complete
       sequence [Homo sapiens]
(full-length)
Human HIP2          11      12      gb|AC007245.3|AC007245 Homo sapiens BAC clone
       RP11-273L18 from 7, complete sequence
(full-length)
Human HIP2          11      12      gb|AC007999.11|AC007999 Homo sapiens 3q25-26
       BAC CTB-177N7 (California Institute of Technology BAC
(full-length)                       Library) complete sequence
Human HIP2          11      12      gb|AC015801.25|AC015801 Homo sapiens chromosome
       17, clone RP11-854A13, complete sequence
(full-length)
Human HIP2          11      12      gb|AF083127.1|AF083127 Homo sapiens CATX-11
       mRNA, partial cds
(full-length)
Human HIP2          11      12      gb|AF161453.1|AF161453 Homo sapiens HSPC335
       mRNA, partial cds
(full-length)
Human HIP2          11      12      gb|AF180425.2|AF180425 Homo sapiens
       retinoblastoma-associated protein RAP140 mRNA, complete cds
(full-length)
Human HIP2          11      12      gb|AF307339.1|AF307339 Homo sapiens B
       aggressive lymphoma short isoform (BAL) mRNA, omplete cds
(full-length)
Human HIP2          11      12      ref|NM_000304.1| Homo sapiens peripheral myelin
       protein 22 (PMP22), mRNA
(full-length)
Human HIP2          11      12      ref|NM_001034.1| Homo sapiens ribonucleotide
       reductase M2 polypeptide (RRM2), mRNA
(full-length)
Human HIP2          11      12      ref|NM_001282.1| Homo sapiens adaptor-related
       protein complex 2, beta 1 subunit (AP2B1), mRNA
(full-length)
Human HIP2          11      12      ref|NM_001634.3| Homo sapiens
       S-adenosylmethionine decarboxylase 1 (AMD1), mRNA
(full-length)
Human HIP2          11      12
IT     475603-56-6   475612-39-6   475612-40-9   475612-41-0   475617-37-9
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475618-57-6 475618-58-7 **475618-59-8** 475618-60-1
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475618-81-6 475618-82-7 475618-83-8 475618-84-9 475618-85-0
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475619-60-4 475619-61-5 475619-62-6 475619-63-7 475619-64-8
475619-65-9 475619-66-0
(amino acid sequence; protein-protein interaction domains of adipocyte proteins and method for screening for assocn.-inhibiting drugs)

IT 475619-67-1 475619-68-2 475619-69-3 475619-70-6 475619-71-7
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475619-87-5 475619-88-6 475619-89-7 475619-90-0 475619-91-1
475619-92-2 475619-93-3 475619-94-4 475619-95-5 **475619-96-6**
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475620-37-2 475620-38-3 **475620-39-4** 475620-40-7
475620-41-8 475620-42-9 475620-43-0 475620-44-1 475620-45-2
475620-46-3 475620-47-4 475620-48-5 475620-49-6 475620-50-9
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475620-66-7 475620-67-8 475620-68-9 475620-69-0 475620-70-3
475620-71-4 475620-72-5 475620-73-6 475620-74-7 475620-75-8
475620-76-9 475620-77-0 475620-78-1 **475620-79-2**
475620-80-5 475620-81-6 475620-82-7 475620-83-8 475620-84-9
475620-85-0 475620-86-1 475873-65-5 475873-66-6 475873-67-7
475873-68-8 475873-69-9 475873-70-2 475873-71-3 475873-72-4
475873-73-5 475873-74-6
(amino acid sequence; protein-protein interaction domains of adipocyte proteins and method for screening for assocn.-inhibiting drugs)

L16 ANSWER 5 OF 22 USPATFULL on STN
AN 2003:318639 USPATFULL
TI Atherosclerotic phenotype determinative genes and methods for using the same
IN West, Mike, Durham, NC, UNITED STATES

Nevins, Joseph R., Chapel Hill, NC, UNITED STATES
Goldschmidt, Pascal, Chapel Hill, NC, UNITED STATES
PI US 2003224383 A1 20031204
AI US 2002-291885 A1 20021112 (10)
PRAI US 2002-374547P 20020423 (60)
US 2002-420784P 20021024 (60)
US 2002-421043P 20021025 (60)
US 2002-424680P 20021108 (60)
DT Utility
FS APPLICATION
LREP Gregory J. Glover, Ropes & Gray, Suite 800 East, 1301 K Street, NW, Washington, DC, 20005
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 235 Drawing Page(s)
LN.CNT 2165
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0169] The genes identified as having discriminatory expression code for both known proteins and others whose annotation has not been established. Some of the genes, such **apolipoprotein** E (apoE) and osteopontin, have been previously associated with atherosclerosis. Another group of genes code for proteins that belong to categories that one would expect from a survey of atherosclerotic tissue but have not been directly linked to atherosclerosis. Genes in this category belong to inflammatory, growth signaling, and cell-cell communication pathways. Interesting and unexpected candidates include genes such as chemokine receptor (CXCR4) and E2F transcription factor 6 (E2F-6).
DETD [0177] Finally, this methodology has identified a number of clinically relevant candidate genes that encode proteins whose function is consistent with a role in atherosclerosis, such as proteins belonging to inflammatory, growth signaling, and cell-cell communication pathways. Some of these genes such as apoE, ER-.beta. and osteopontin have previously been directly associated with atherosclerosis. The apoE gene and particularly apoE gene variants, have been linked to the development of atherosclerosis in humans. See Ilveskoski E, Perola M, Lehtimaki T, et al. Agedependent association of **apolipoprotein** E genotype with coronary and aortic atherosclerosis in middle-aged men: an autopsy study. Circulation 1999; 100:608-13. In these studies, apoE gene expression was elevated in the high susceptibility sections. While primarily expressed in the liver and the brain, apoE is also expressed in monocytes and vascular smooth muscle cells where it may play a role in paracrine and autocrine cholesterol transport, and induce smooth muscle cell differentiation and proliferation. See Mahley R W. **Apolipoprotein** E: cholesterol transport protein with expanding role in cell biology. Science 1988; 240:622-30.
IT 444952-62-9 444952-63-0 444952-64-1 444952-70-9, Protein (human 534-amino acid) 444952-83-4 444952-87-8 444953-00-8 444953-49-5 444953-63-3 444953-68-8, Protein (human 3261-amino acid) 444953-70-2, Glycogen synthase kinase 3 (human) 444954-01-2, Zinc finger protein (human gene znfmf) 444954-15-8, Protein (human gene BCL7A) 444954-26-1 444954-51-2 444955-57-1 444955-73-1 444956-01-8, Thrombospondin 2 (human gene THBS2) 444956-35-8 444956-44-9, FRAP-related protein (human gene FRP1) 444956-50-7 444956-76-7 444956-96-1 444956-97-2, Protein (human gene BS69) 444967-29-7 444967-46-8 444967-51-5, P115 (human cell line HepG2) 444967-53-7 444967-60-6 444967-69-5, Protein (human 598-amino acid) 444967-71-9, Protein (human 772-amino acid) 444968-12-1 444968-13-2 444968-14-3 444968-15-4 444968-16-5 444968-17-6 444968-22-3, ATP-dependent RNA helicase #46 (human) **444968-28-9**, Protein (human gene FN1) 444985-02-8 444985-11-9 444985-12-0, MIHB (human gene MIHB) 445046-96-8 445047-00-7 445047-03-0 445047-08-5 445047-18-7 445047-25-6 445047-26-7 445047-28-9 459481-13-1 459483-00-2, GenBank AAA35519 459483-09-1, GenBank AAB05827 459484-84-5, GenBank AAA63256 459485-04-2 459488-70-1, GenBank CAB46206 459490-09-6

459493-10-8, GenBank BAA24902 459501-82-7 459502-37-5 459502-62-6, GenBank AAC50780 459503-44-7, Transcription factor (human gene LOT1) 459503-76-5 459503-96-9, GenBank CAA70103 459504-99-5, GenBank AAC14197 459505-47-6, GenBank AAC18133 459506-16-2, GenBank BAA76770 459509-52-5, GenBank CAB45718 459512-33-5, Prointerleukin-1-beta (human) 459512-37-9, GenBank AAB51316 459512-55-1, GenBank AAB51309 459512-77-7, GenBank CAA27291 459513-03-2 459513-65-6, GenBank AAA61182 459514-21-7, Interleukin 8 (human gene IL8) 459514-38-6, Interleukin 3 (human gene IL3) 459514-40-0, GenBank BAA00733 459514-62-6, GenBank AAA64919 459515-10-7, GenBank CAB05109 459515-19-6, GenBank AAB21188 459515-75-4, Protein (human gene SPARC) 459515-98-1 459517-16-9, GenBank CAA32889 459517-42-1, GenBank AAA59883 459517-92-1, GenBank CAB42843 459517-97-6, GenBank AAB51320 459518-75-3, GenBank AAA60964 459518-86-6, GenBank AAA52582 459518-87-7, GenBank AAB51313 459519-31-4 459519-36-9, GenBank AAB40115 459519-47-2, GenBank CAA38401 459519-62-1, GenBank CAA38139 459519-86-9 459520-58-2, GenBank AAC32887 459520-60-6, GenBank AAA03652 459520-85-5, GenBank AAA35537 459521-00-7, GenBank CAA39840 459521-93-8, GenBank AAA58430 459522-07-7, GenBank AAA35860 459522-09-9 459522-20-4 459522-58-8, GenBank BAA01050 459522-82-8, GenBank CAA11277 459522-84-0 459522-94-2, GenBank CAA40016 459522-98-6, HLA-DMB (human) 459523-06-9, GenBank AAC78725 459523-07-0, GenBank CAA41226 459523-95-6, GenBank AAB51323 459524-17-5, Protein (human gene PGM1) 459525-01-0, Proteinase inhibitor elafin (human) 459525-21-4 459526-33-1 459526-46-6, GenBank CAA49189 459527-53-8, GenBank AAA60084 459527-85-6, GenBank BAA02185 459528-84-8, GenBank CAA40623 459529-97-6, GenBank AAB59361 459530-14-4, GenBank AAA59991 459530-33-7, GenBank AAB03814 459530-46-2, GenBank AAB02790 459530-52-0, GenBank BAA04480 459530-81-5, GenBank CAA53091 459531-41-0, Ceramidase, glucosyl- (human gene GBA) 459531-47-6, GenBank AAA56833 459532-04-8, GenBank CAA79696 459532-55-9, GenBank AAA36443 459533-15-4 459533-28-9 459533-91-6 459534-79-3, GenBank AAA59187 459535-11-6, Protein p84 (human clone N5-4) 459535-52-5 459535-67-2, GenBank AAB88724 459536-05-1, GenBank BAA02804 459536-28-8, GenBank AAA81905 459536-49-3, BST-1 precursor (human clone BST-1) 459536-64-2, GenBank AAC41994 459536-84-6, GenBank AAA36033 459536-88-0 459536-92-6 459537-01-0 459537-18-9, Protein HFcRn (human clone 11/3) 459537-34-9, GenBank AAA91631 459537-57-6, GenBank CAA99732 459537-97-4, GenBank BAA06684 459538-63-7 459538-79-5, Calgizzarin (human cell line COLO 205) 459539-00-5, GenBank CAA63224 459539-88-9, GenBank AAC50820 459540-22-8, GenBank AAC50155 459542-16-6, Protein (human clone 126 gene DR-nm-23) 459542-25-7, TBX2 (human gene TBX2) 459542-26-8 459542-79-1, GenBank AAC50205 459543-02-3, GenBank AAA91458 459543-17-0, GenBank CAA65633 459543-67-0, GenBank AAC34294 459543-68-1, GenBank AAB36088 459548-54-0 459548-69-7, GenBank AAC41939 459549-72-5, GenBank AAC34293 459549-73-6, GenBank CAA90626 459550-13-1, GenBank AAC50461 459550-74-4, P126 (Human gene ST5) 459550-78-8, GenBank AAA99014 459551-69-0, GenBank AAC63952 459551-98-5, GenBank CAB46207 459552-30-8, Sodium channel 1 (human gene hBNaC1) 459552-49-9, Metaxin (human) 459552-61-5, GenBank AAB51310 459552-63-7, GenBank AAB51311 459552-64-8, GenBank AAB51312 459552-66-0, GenBank AAB51315 459552-68-2, GenBank AAB51314 459552-75-1, GenBank CAA04888 459552-77-3, GenBank AAB07788 459552-80-8, GenBank AAA98672 459553-40-3, GenBank AAC50512 459553-43-6 459553-76-5, GenBank AAC50555 459553-79-8, GenBank BAA12351 459554-37-1, Protein (human gene PEA-15) 459554-42-8, GenBank AAC97927 459554-67-7, GenBank AAB17545 459554-94-0 459555-32-9, Cofactor C (human) 459555-98-7, GenBank AAC50599 459556-46-8, GenBank AAB07119 459556-65-1, Protein (human gene DUSP6) 459556-71-9, GenBank BAA20383 459557-24-5, GenBank AAC24308 459557-27-8 459562-52-8, GenBank BAA11419 459562-85-7, GenBank AAC50695 459573-33-2, GenBank BAA21817 459576-99-9, PIG-B (human cell line P39) 459577-55-0, GenBank CAA66942 459577-66-3, GenBank AAC50786

459578-04-2 459579-01-2 459579-29-4, GenBank CAA57478 459579-60-3, GenBank BAA13392 459579-92-1 459580-08-6, Protein CGR19 (human clone hCGR19) 459580-28-0, GenBank BAA13322 459580-64-4, GenBank AAC24306 459581-12-5, Protein (human gene OLF3) 459582-00-4, GenBank AAB42217 459582-06-0, GenBank AAB41495 459582-49-1 459582-56-0, Tub (human) 459584-51-1 459585-20-7, GenBank AAC24307 459585-33-2, GenBank AAC34273 459585-71-8 459585-75-2, GenBank CAA67896 459585-79-6, Myosin I beta (human) 459585-90-1, GenBank AAB51327 459585-91-2, GenBank AAB51328 459585-92-3, GenBank AAB51319 459585-93-4, GenBank AAB51321 459585-95-6, GenBank AAB51325 459585-96-7, GenBank AAC51640 459585-97-8, GenBank AAB51326 459586-22-2 459586-61-9, GenBank CAA65480 459586-81-3 459587-14-5, GenBank AAC13869 459587-17-8, GenBank AAC39893 459587-73-6, GenBank AAC51233 459587-96-3, GenBank AAB41838 459588-41-1, GenBank CAA71138 459588-75-1, GenBank AAB53091 459588-94-4, GenBank CAA71669 459589-43-6, GenBank AAB60859 459589-51-6, GenBank BAA20772
(amino acid sequence; genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics)

IT 462375-10-6, GenBank CAB42830 462506-52-1, GenBank AAC82375 462531-18-6 462693-44-3, P115 (human clone E1,E2 gene C1) 462693-96-5, Protein (human gene hCDC10) 462694-08-2 468850-40-0 473526-57-7 473526-63-5 475132-53-7 475132-67-3 475229-10-8 475229-23-3, Ferritin (human heavy chain) 475229-25-5, Hnrnp a1 protein (human clone pES5) 475229-26-6, Prosaposin (human gene GLBA) 475229-41-5, .alpha.-D-galactosidase A (human gene GLA) 475229-42-6 475229-43-7 475229-44-8 475310-87-3, Complement factor B (human) 476273-90-2, Smoothelin (human gene SMTN isoform B) 477273-16-8, Type IV collagenase (human gene CLG4A) 477273-85-1, GenBank BAA07892 479325-19-4 479325-20-7 479325-21-8 479325-23-0, G7b protein (human gene G7b) 479325-72-9, GenBank CAA51999 479325-77-4, Protein (human gene muf1) 479325-84-3, PINCH protein (human clone cPINCH 1) 479327-92-9 479327-93-0 479327-94-1 479327-95-2, UPKA (human clone R31396-F25451-R31076) 479328-09-1, GenBank CAA38101 479328-11-5, Protein (human gene ADE2H1) 479328-18-2, GenBank CAA47144 479328-31-9 479328-36-4 479328-38-6 479328-47-7 479328-49-9, HNop56 (human cell line Hela) 479328-54-6, GenBank CAA71216 479329-10-7, Fumarase precursor (human gene FH) 479329-32-3 479329-35-6 479329-36-7, GenBank AAC50564 479329-41-4 479329-68-5 479329-69-6, GenBank BAA31629 479329-75-4, GenBank BAA22953 479329-76-5 479329-83-4, Protein (human gene ZAKI-4) 479329-84-5 479329-87-8 479329-89-0 479329-94-7, Osteonidogen (human) 479329-97-0 479330-03-5, ORF (human cell line KG-1 gene KIAA0035) 479330-07-9 479330-08-0 479330-10-4 479330-11-5 479330-12-6 479330-16-0 479330-17-1, GenBank BAA13217 479330-39-7, Selenium donor protein (human gene selD) 479330-40-0, GenBank AAA99722 479330-43-3 479330-44-4, Threonyl-tRNA synthetase (human) 479330-57-9, GenBank AAB39369 479330-72-8, Acyl-CoA dehydrogenase (human gene SCAD) 479330-74-0, Protein (human 500-amino acid) 479330-75-1, Cu++-transporting P-type ATPase (human) 479330-78-4, Nucleotide binding protein (human) 479330-79-5, Nerve growth factor (human gene HBNF-1) 479330-84-2, GenBank BAA25471 479330-85-3 479331-09-4 479331-23-2 479474-93-6, Protein (human 415-amino acid) 479475-05-3, GenBank CAA08987 479475-10-0 479475-11-1 479475-17-7, GenBank AAA68980 479475-23-5, GenBank CAA47001 479475-24-6 479475-29-1 479475-59-7 479476-00-1, Glutaredoxin (human gene grx) 479476-39-6, Dodecenoyl-CoA delta-isomerase (human) 479476-42-1, GAIP (human cell line HeLa S3) 479476-61-4, GenBank AAB47133 479476-64-7, GenBank AAB59360 479476-67-0, GenBank CAA25137 479476-81-8, GenBank AAC27120 479476-84-1 479476-90-9 479477-37-7, Tic (human gene TIC) 479477-43-5 479477-57-1, HSRP1alpha (human cell line HeLa) 479477-65-1, GenBank BAA11179 479477-66-2 479477-67-3 479477-71-9, Protein (human clone 39H11 gene LLGL) 479477-73-1 479477-80-0 479478-12-1, GenBank AAA98529 479478-13-2, GenBank AAA99716 479478-14-3, GenBank AAA99717 479478-23-4, GenBank AAB34635

479478-24-5 479478-31-4, Thrombospondin-1p180 (human) 479478-32-5, GenBank AAA21126 479478-33-6, Protein (human clone I1, D1 gene ZP3) 479478-35-8, GenBank AAA35678 479478-44-9, GenBank AAA36193 479478-54-1 479478-56-3, Protein (human gene IGF1R) 479478-59-6 479478-63-2, Mannose receptor (human gene MRC1) 479478-65-4 479478-71-2 479659-73-9, GenBank CAA77082 479659-98-8, GenBank CAA17876 479659-99-9, GenBank CAA17877 479660-00-9, GenBank CAA17878 479660-01-0, GenBank CAA17879 479660-02-1, GenBank CAA17880 479660-05-4, GenBank CAA09626 479660-47-4 479660-60-1, Dead box, X isoform (human gene DBX) 479660-72-5, Esterase D (human) 479660-78-1, GenBank BAA04231 479660-79-2 **479660-93-0**, Fibronectin precursor (human) 479660-95-2 479660-96-3, GenBank AAA36777 479797-46-1, GenBank CAA04167 479798-17-9 479798-41-9, GenBank CAB10840 479798-42-0, GenBank CAB10841 479800-13-0, GenBank AAL76125 479800-16-3, GenBank AAA51775 479800-32-3, Cardiotrophin-1 (human gene CTF1) 479800-35-6 479841-23-1 479849-27-9 479850-80-1, Protein (human clone 640 131-amino acid) 479857-40-4 479859-03-5 479864-78-3 479864-79-4 479915-99-6 479921-73-8 479922-21-9 479922-42-4, Butyrophilin (human gene BTF5) 479957-30-7 479959-20-1 479959-21-2 479965-06-5, GenBank CAB57259 479965-47-4, GenBank CAC18785 479965-48-5, GenBank CAB38781 479965-49-6, GenBank CAB38780 479966-04-6 479966-05-7 479966-06-8 479966-07-9 479967-04-9, Protein (human 792-amino acid) 479967-25-4, GenBank CAA48833 479967-32-3, GenBank CAB42888 479967-33-4, GenBank CAB42889 479967-34-5, GenBank CAB42890 479967-35-6, GenBank CAB42892 479967-36-7, GenBank CAB42893 479967-47-0 479967-48-1 479967-49-2 479968-13-3, GenBank CAB43745 479970-17-7, GenBank CAB42562 479970-26-8, GenBank CAA21140 479970-28-0, GenBank CAA21141 479970-79-1 479970-80-4 479971-64-7, GenBank AAA16174 479971-85-2, GenBank CAA20116 479971-86-3, GenBank CAA20117 479971-87-4, GenBank CAA20118 479971-88-5, GenBank CAA20119 479971-89-6, GenBank CAA20120 479971-90-9 479971-91-0 479971-92-1 479972-23-1 479972-26-4 479972-27-5 479972-29-7, GenBank CAA20344 479972-30-0, GenBank CAA20345 479972-31-1, GenBank CAA20346 479972-32-2, GenBank CAA20347 479972-33-3, GenBank CAA20350 479972-34-4, GenBank CAA20349 479972-35-5, GenBank CAA20348 479972-36-6, GenBank CAA20351 479972-37-7, GenBank CAA20352 479972-38-8, GenBank CAA20354 479972-39-9, GenBank CAA20355 479972-40-2, GenBank CAA20356 479972-41-3, GenBank CAB40157 479972-42-4, GenBank CAB40158 479972-43-5, GenBank CAB40159 479972-44-6, GenBank CAB40160 479973-07-4 479973-08-5 479973-09-6 479973-10-9 479973-11-0 479973-12-1 479973-13-2 479973-14-3 479973-15-4 479973-16-5 479973-17-6 479973-18-7 479973-19-8 479973-67-6, GenBank CAB16203 479974-44-2, Protein (human 2701-amino acid) 479974-62-4, Protein (human clone 612B18) 479979-47-0, GenBank CAB46442 479986-58-8 479990-59-5, Protein (human 137-amino acid) 479990-72-2 479993-95-8 479995-88-5, GenBank CAA76877 479995-99-8 480000-09-7 480000-14-4 480000-30-4, GenBank CAB51604
(amino acid sequence; genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics)

L16 ANSWER 6 OF 22 USPATFULL on STN
AN 2003:312163 USPATFULL
TI Diagnostic and prognostic tests
IN Gordon, Gavin J., Brighton, MA, UNITED STATES
Jensen, Roderick V., Pelham, CT, UNITED STATES
Gullans, Steven R., Natick, MA, UNITED STATES
Bueno, Raphael, Brookline, MA, UNITED STATES
PA The Brigham and Women's Hospital, Inc., Boston, MA (U.S. corporation)
PI US 2003219760 A1 20031127
AI US 2002-236031 A1 20020905 (10)
PRAI US 2001-317389P 20010905 (60)
US 2002-407431P 20020830 (60)
DT Utility

FS APPLICATION
LREP John R. Van Amsterdam Ph.D., Esq., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 82
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 4585
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0210]
TABLE 7

Symbol	Description
BF	B-factor, properdin
MSLN	mesothelin
TM4SF1	transmembrane 4 superfamily member 1
CYC1	cytochrome c-1
RPL12	ribosomal protein L12
POLR2L	polymerase (RNA) II (DNA directed) polypeptide L (7.6 kD)
RPL18	ribosomal protein L18
RPL18A	ribosomal protein L18a
RPS23	ribosomal protein S23
RPS21	ribosomal protein S21
RPL27	ribosomal protein L27
K-ALPHA-1	tubulin, alpha, ubiquitous
ARHGAP1	Rho GTPase activating protein 1
TPM1	tropomyosin 1 (alpha)
APOL	**apolipoprotein** L
TPM1	tropomyosin 1 (alpha)
SPARC	secreted protein, acidic, cysteine-rich (osteonectin)
COL1A2	collagen, type I, alpha 2
FN1	fibronectin 1
NA	Fibronectin, Alt. Splice 1
FN1	fibronectin 1
COL5A2	collagen, type V, alpha 2
COL1A2	collagen, type I, alpha 2
ACTA2	actin, alpha2, smooth muscle, aorta
TAGLN	transgelin

DETD [0314] Training Set (Beer et al. data); good outcome (n=21) means alive at 5 years; poor outcome (n=11) means disease recurrence within 4 years.
TABLE 13

Genes overexpressed in tumors of different outcome

Gene #	Overexpressed in . . .	Locus Link Symbol	Accession #	Description
1	Good	APOE	M12529	**apolipoprotein** E
4	Good	LPIN2	D87436	lipin 2
5	Poor	SLC2A1	K03195	solute carrier family 2 (facilitated glucose trans-porter), member 1
6	Poor	S100P	AA131149	S100 calcium-binding protein P
7	Poor	MST1R	X70040	macrophage stimulating 1 receptor (c-met-related tyrosine kinase)

IT 501985-47-3, Synthetase, prostacyclin (human) 501985-49-5, Ladinin 1 (human) 501985-51-9, CD antigen, CD24 (human) 501985-53-1 501985-55-3, Protein (human upregulated by BCG-CWS) 501985-57-5, Complement factor B (human) 501985-59-7, Transgelin (human) 501985-61-1 501985-63-3, Myosin (human light chain 6) 501985-65-5, Integrin .alpha.5 (human) 501985-67-7, Moesin (human) 501985-69-9, Dynein (human) 501985-71-3, Protein (human gene KIAA0685) 501985-82-6, Protein (human IMAGE clone 280506) 501985-83-7, Riboomal protein L34 (human) 501985-84-8, Protein (human clone PAC6802) 501985-85-9, Biglycan (human) **501985-86-0**, Fibronectin (human) 501985-87-1, Collagen VI (human) 501985-88-2, Procollagen .alpha.2(V) (human) 501985-89-3, Protein MAC25 (human) 501985-90-6, Actin (human .alpha. subunit) 501985-91-7, Immunoglobulin receptor, IgG2a (human) (amino acid sequence; gene expression profiling in diagnosis and prognosis of cancer)

L16 ANSWER 7 OF 22 USPATFULL on STN
AN 2003:282611 USPATFULL
TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE (non-U.S. corporation)
PI US 2003198954 A1 20031023
AI US 2001-1142 A1 20011114 (10)
RLI Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING
PRAI WO 2001-IB1715 20010806
US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)
DT Utility
FS APPLICATION
LREP SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, 2421 N.W. 41ST STREET, SUITE A-1, GAINESVILLE, FL, 326066669
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25681
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0542] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL, chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.
DETD [0994] In a further embodiment, the present protein provides a method to purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using

the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.

DETD [1164] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amyloidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein.

DETD [1325] The cDNA of Clone 646477.sub.--181-19-2-0-F4-F (SEQ ID NO:105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO:106, comprising the amino acid sequence: MISPVLILFSSFLCHVAIAGRTCPKPDDLPFSTVVP LKTFYEPGEEITYSCKPGYVSRGGMRK FICPLTGLWLINTLKCTPRVCPFAGILENGAVRYTTFEYPNTIS FSCNTGFYLNGADSAKCT EEGKWSPELPVCAPIICPPPSIPTFATLRVYKPSAGNNSLYRDTAVFECLPQH AMFGNDTIT CTTHGNWTKLPECREVKCPFPSRPDNGFVNYPAKPTLYYKDKATFGCHDGYSLDGPEEIE CTKLGNWSAMPSCKASCKVPVKKATVVYQGERVKIQEKFKNGMLHGDKVSFFCKNKEK KCSYTEDAQCIDGTIEVPKCFKEHSSLAFWKTDASDVKPC. Accordingly, it will be appreciated that all characteristics and uses of the polypeptides of SEQ ID NO:106 described throughout the present application also pertain to the polypeptides encoded by the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. In addition, it will be appreciated that all characteristics and uses of the polynucleotides of SEQ ID NO:105 described throughout the present application also pertain to the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. A preferred embodiment of the invention is directed toward the compositions of SEQ ID NO:105, SEQ ID NO:106, and Clone 646477.sub.--181-19-2-0-F4-F. Also preferred are polypeptide fragments having a biological activity as described herein and the polynucleotides encoding the fragments.

DETD [1326] The protein of SEQ ID NO:106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession numberP02749). Like apoliprotein H, the protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi 3), amino acids 205 to 260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO:106, is highly expressed in liver.

DETD [1327] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOH) may prevent activation of the

intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell-humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase acitvity of platelets. NAPOH exerts multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1328] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO:106.

DETD [1698] Antibody preparations prepared according to either the monoclonal or the polyclonal protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

TABLE I

SEQ ID NO.	Sequence Type	ATCC Deposit	ATCC Clone ID_Clone Name	ATCC Deposit Date	Name
1	DNA	PTA-2732	223583_114-044-2-0-E11-F	Nov. 27, 2000	S-100A10rP
2	Protein	PTA-2732	223583_114-044-2-0-E11-F	Nov. 27, 2000	S-100A10rP
3	DNA	PTA-2732	1000848582_181404-0-A11-F	Nov. 27, 2000	SCPhx
4	Protein	PTA-2732	1000848582_18140-4-0-A11-F	Nov. 27, 2000	SCPhx
5	DNA	PTA-2732	1000839315_220-26-1-0-F3-F	Nov. 27, 2000	Chimerin
6	Protein	PTA-2732	1000839315_220-26-1-0-F3-F	Nov. 27, 2000	Chimerin
7	DNA		1000770704_208-27-3-0-G6-F		Ca1X

			protein (hJNK3-BP)
109	DNA	231462_117-065-1-0-G11-F	DROCK2
110	Protein	231462_117-065-1-0-G11-F	DROCK2
111	DNA	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)
112	Protein	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 8 OF 22 USPATFULL on STN
AN 2003:250925 USPATFULL
TI Molecular antigen array
IN Renner, Wolfgang A., Zurich, SWITZERLAND
Bachmann, Martin, Winterthur, SWITZERLAND
Tissot, Alain, Zurich, SWITZERLAND
Maurer, Patrick, Winterthur, SWITZERLAND
Lechner, Franziska, Zurich, SWITZERLAND
Sebbel, Peter, Zurich, SWITZERLAND
Piossek, Christine, Winterthur, SWITZERLAND
Ortmann, Rainer, Saint Louis, SWITZERLAND
Luond, Rainer, Therwil, SWITZERLAND
Staufenbiel, Matthias, Lorrach, GERMANY, FEDERAL REPUBLIC OF
Frey, Peter, Bern, SWITZERLAND
PA Cytos Biotechnology AG (non-U.S. corporation)
PI US 2003175711 A1 20030918
AI US 2002-50898 A1 20020118 (10)
PRAI US 2001-331045P 20011107 (60)
US 2001-326998P 20011005 (60)
US 2001-288549P 20010504 (60)
US 2001-262379P 20010119 (60)
DT Utility
FS APPLICATION
LREP STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., WASHINGTON, DC, 20005
CLMN Number of Claims: 53
ECL Exemplary Claim: 1
DRWN 54 Drawing Page(s)
LN.CNT 14673
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0014] As indicated, one of the key events in Alzheimer's Disease (AD) is the deposition of amyloid as insoluble fibrous masses (amyloidogenesis) resulting in extracellular neuritic plaques and deposits around the walls of cerebral blood vessels (for review see Selkoe, D. J. (1999) Nature. 399, A23-31). The major constituent of the neuritic plaques and congophilic angiopathy is amyloid .beta. (A.beta.),

although these deposits also contain other proteins such as glycosaminoglycans and **apolipoproteins**. A.beta. is proteolytically cleaved from a much larger glycoprotein known as Amyloid Precursor Proteins (APPs), which comprises isoforms of 695-770 amino acids with a single hydrophobic transmembrane region. A.beta. forms a group of peptides up to 43 amino acids in length showing considerable amino- and carboxy-terminal heterogeneity (truncation) as well as modifications (Roher, A. E., Palmer, K. C., Chau, V., & Ball, M. J. (1988) J. Cell Biol. 107, 2703-2716. Roher, A. E., Palmer, K. C., i, E. C., Ball, M. J., & Greenberg, B. D. (1993) J. Neurochem. 61, 1916-1926). Prominent isoforms are A.cndot. 1-40 and 1-42. It has a high propensity to form 1-sheets aggregating into fibrils, which ultimately leads to the amyloid. Recent studies demonstrated that a vaccination-induced reduction in brain amyloid deposits resulted in cognitive improvements (Schenk, D., Barbour, R., Dunn, W., Gordon, G., Grajeda, H., Guido, T., Hu, K., Huang, J., Johnson-Wood, K., Khan, K., et al. (1999) Nature. 400, 173-177).

IT 444038-99-7P, Antigen 1 (hepatitis B virus) 444039-00-3P, Antigen 2 (hepatitis B virus) 444039-01-4P, Antigen 3 (hepatitis B virus) 444039-02-5P, Antigen 4 (hepatitis B virus) 444039-03-6P, Antigen 5 (hepatitis B virus) 444039-04-7P, Antigen 6 (hepatitis B virus) 444039-05-8P, Antigen 7 (hepatitis B virus) 444039-06-9P, Antigen 8 (hepatitis B virus) 444039-07-0P, Antigen 9 (hepatitis B virus) 444039-08-1P, Antigen 10 (hepatitis B virus) 444039-09-2P, Antigen 11 (hepatitis B virus) 444039-10-5P, Antigen 12 (hepatitis B virus) 444039-11-6P, Antigen 13 (hepatitis B virus) 444039-12-7P, Antigen 14 (hepatitis B virus) 444039-13-8P, Antigen 15 (hepatitis B virus) 444039-14-9P, Antigen 16 (hepatitis B virus) 444039-16-1P, Pilus type 1 (Escherichia coli) 444039-18-3P, Antigen 17 (hepatitis B virus) 444039-19-4P, Antigen 18 (hepatitis B virus) 444039-20-7P, Protein (Enterobacteria phage Q.beta.) 444039-21-8P, Protein (Enterobacteria phage R17) 444039-22-9P, Protein (Enterobacteria phage fr) 444039-23-0P, Protein (Enterobacteria phage GA) 444039-24-1P, Protein (Enterobacteria phage SP) 444039-25-2P, Protein (Enterobacteria phage MS2) 444039-26-3P, Protein (Enterobacteria phage M11) 444039-27-4P, Protein (Enterobacteria phage MX1) 444039-28-5P, Protein (Enterobacteria phage NL95) 444039-29-6P 444039-30-9P 444039-31-0P, Phospholipase A2 (Apis dorsata fragment) 444039-32-1P, Phospholipase A2 (Apis cerana fragment) 444039-33-2P 444039-34-3P 444039-35-4P 444039-36-5P 444039-37-6P, Immunoglobulin E (human heavy chain) 444039-43-4P, Phospholipase A2 (synthetic) 444039-44-5P 444039-45-6P 444039-46-7P 444039-47-8P 444039-48-9P, Cytokine MIF (rat fragment) 444039-49-0P, Cytokine MIF (mouse fragment) 444039-50-3P, Cytokine MIF (human fragment) 444039-51-4P, Interleukin 17 (human) 444039-52-5P, Interleukin 17 (mouse) 444039-53-6P, Interleukin 13 (human precursor) 444039-54-7P, Interleukin 13 (human) 444039-55-8P, Interleukin 13 (mouse) 444039-56-9P, Interleukin 5 (human precursor) 444039-57-0P, Interleukin 5 (human) 444039-58-1P, Interleukin 5 (mouse) 444039-59-2P 444039-60-5P 444039-61-6P 444039-62-7P 444039-64-9P, Eotaxin 1 (human) 444039-65-0P, Eotaxin 2 (human) 444039-66-1P, Eotaxin 3 (human) 444039-67-2P, Eotaxin 1 (mouse) 444039-68-3P, Eotaxin 2 (mouse) 444039-69-4P, Resistin (human precursor) 444039-70-7P, Resistin (mouse precursor) 444039-90-1P 444039-91-2P, 49-306-Lymphotoxin (human) 444039-92-3P, 126-306-Lymphotoxin (human) 444039-93-4P, Protein prion (synthetic human fragment) 444039-94-5P 444039-95-6P, Protein prion (synthetic sheep fragment) 444039-96-7P 444039-97-8P 444039-98-9P 444039-99-0P 444040-00-0P, Resistin C (human fragment) 444040-01-1P 444040-02-2P 444040-03-3P 444040-04-4P 444040-05-5P, Protein met-MIF-C1 (human) 444040-06-6P, Protein MIF-C1 (human) 444040-07-7P, Protein met-MIF-C2 (human) 444040-08-8P, Protein MIF-C2 (human) **444040-09-9P**, Protein met-MIF-C3 (human) **444040-10-2P**, Protein MIF-C3 (human) 444040-11-3P 444040-12-4P, Protein PS-C-RANKL (synthetic human)

(amino acid sequence; vaccine compns. comprising mol. antigen array against cancer, infection, and allergy)

IT 444038-87-3, .beta.-Lymphocyte chemoattractant (mouse) 444039-63-8, .beta.-Lymphocyte chemoattractant (human) 444039-71-8, Lymphotoxin .beta. (human) 444039-72-9, Lymphotoxin .beta. (mouse) 444039-73-0, Protein PP7 (RNA-phage) 444039-74-1, Protein SPA1 (RNA-phage) 444039-75-2, Protein Q.beta.-240 (Enterobacteria phage) 444039-76-3, Protein Q.beta.-243 (Enterobacteria phage) 444039-77-4, Protein Q.beta.-250 (Enterobacteria phage) 444039-78-5, Protein Q.beta.-259 (Enterobacteria phage) 444039-79-6, Protein Q.beta.-251 (Enterobacteria phage) 444039-80-9, Protein C-IL-13-F (mouse) 444039-81-0, Protein C-IL-13-F (human) 444039-82-1, Protein C-IL-13-S (mouse) 444039-83-2, Protein C-IL-13-S (human) **444039-84-3**, Protein C-IL-5-E (mouse) **444039-85-4**, Protein C-IL-5-E (human) 444039-86-5, Protein C-IL-5-F (mouse) 444039-87-6, Protein C-IL-5-F (human) 444039-88-7, Protein C-IL-5-S (mouse) 444039-89-8, Protein C-IL-5-S (human)
(amino acid sequence; vaccine compns. comprising mol. antigen array against cancer, infection, and allergy)

IT 444041-57-0 444041-59-2 444041-61-6 444041-64-9 444041-67-2
444041-81-0 444041-96-7 444042-17-5 444042-18-6 444042-19-7
444042-20-0 444042-21-1 444042-22-2 444042-23-3 444042-24-4
444042-25-5 444042-26-6 444042-27-7 444042-28-8 444042-29-9
444042-30-2 444042-31-3 444042-32-4 444042-33-5 444042-34-6
444042-35-7 444042-36-8 444042-37-9 444042-38-0 444042-39-1
444042-40-4 444042-41-5 444042-42-6 444042-43-7 444042-44-8
444042-45-9 444042-47-1 444042-48-2 444042-49-3 444042-50-6
444042-51-7 444042-52-8 444042-53-9 444042-54-0 444042-55-1
444042-61-9 444042-62-0 444042-69-7 444042-71-1 444042-72-2
444042-73-3 444042-74-4 444042-75-5 444042-76-6 444042-77-7
444042-98-2 444043-18-9 444043-19-0 **444043-20-3**
444043-25-8 444043-26-9 444141-51-9
(unclaimed protein sequence; vaccine compns. comprising mol. antigen array against cancer, infection, and allergy)

L16 ANSWER 9 OF 22 USPATFULL on STN
AN 2003:250504 USPATFULL
TI Molecular antigen array
IN Renner, Wolfgang A., Zurich, SWITZERLAND
Bachmann, Martin, Winterthur, SWITZERLAND
Tissot, Alain, Zurich, SWITZERLAND
Maurer, Patrick, Winterthur, SWITZERLAND
Lechner, Franziska, Zurich, SWITZERLAND
Sebbel, Peter, Zurich, SWITZERLAND
Piossek, Christine, Winterthur, SWITZERLAND
PA Cytos Biotechnology AG (non-U.S. corporation)
PI US 2003175290 A1 20030918
AI US 2002-50902 A1 20020118 (10)
PRAI US 2001-331045P 20011107 (60)
US 2001-326998P 20011005 (60)
US 2001-288549P 20010504 (60)
US 2001-262379P 20010119 (60)
DT Utility
FS APPLICATION
LREP STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., WASHINGTON, DC, 20005
CLMN Number of Claims: 219
ECL Exemplary Claim: 1
DRWN 54 Drawing Page(s)
LN.CNT 15306
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0014] As indicated, one of the key events in Alzheimer's Disease (AD) is the deposition of amyloid as insoluble fibrous masses (amyloidogenesis) resulting in extracellular neuritic plaques and deposits around the walls of cerebral blood vessels (for review see

Selkoe, D. J. (1999) Nature. 399, A23-31). The major constituent of the neuritic plaques and congophilic angiopathy is amyloid .beta. (A.beta.), although these deposits also contain other proteins such as glycosaminoglycans and **apolipoproteins**. A.beta. is proteolytically cleaved from a much larger glycoprotein known as Amyloid Precursor Proteins (APPs), which comprises isoforms of 695-770 amino acids with a single hydrophobic transmembrane region. A.beta. forms a group of peptides up to 43 amino acids in length showing considerable amino- and carboxy-terminal heterogeneity (truncation) as well as modifications (Roher, A. E., Palmer, K. C., Chau, V., & Ball, M. J. (1988) J. Cell Biol. 107, 2703-2716. Roher, A. E., Palmer, K. C., Yurewicz, E. C., Ball, M. J., & Greenberg, B. D. (1993) J. Neurochem. 61, 1916-1926). Prominent isoforms are A.cndot. 1-40 and 1-42. It has a high propensity to form 1-sheets aggregating into fibrils, which ultimately leads to the amyloid. Recent studies demonstrated that a vaccination-induced reduction in brain amyloid deposits resulted in cognitive improvements (Schenk, D., Barbour, R., Dunn, W., Gordon, G., Grajeda, H., Guido, T., Hu, K., Huang, J., Johnson-Wood, K., Khan, K., et al. (1999) Nature. 400, 173-177).

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met-MIF-C3 (human) **444040-10-2P**, Protein MIF-C3 (human)
444040-11-3P 444040-12-4P, Protein PS-C-RANKL (synthetic human)
(amino acid sequence; vaccine compns. comprising mol. antigen array against cancer, infection, and allergy)

IT 444038-87-3, .beta.-Lymphocyte chemoattractant (mouse) 444039-63-8, .beta.-Lymphocyte chemoattractant (human) 444039-71-8, Lymphotoxin .beta. (human) 444039-72-9, Lymphotoxin .beta. (mouse) 444039-73-0, Protein PP7 (RNA-phage) 444039-74-1, Protein SPA1 (RNA-phage) 444039-75-2, Protein Q.beta.-240 (Enterobacteria phage) 444039-76-3, Protein Q.beta.-243 (Enterobacteria phage) 444039-77-4, Protein Q.beta.-250 (Enterobacteria phage) 444039-78-5, Protein Q.beta.-259 (Enterobacteria phage) 444039-79-6, Protein Q.beta.-251 (Enterobacteria phage) 444039-80-9, Protein C-IL-13-F (mouse) 444039-81-0, Protein C-IL-13-F (human) 444039-82-1, Protein C-IL-13-S (mouse) 444039-83-2, Protein C-IL-13-S (human) **444039-84-3**, Protein C-IL-5-E (mouse) **444039-85-4**, Protein C-IL-5-E (human) 444039-86-5, Protein C-IL-5-F (mouse) 444039-87-6, Protein C-IL-5-F (human) 444039-88-7, Protein C-IL-5-S (mouse) 444039-89-8, Protein C-IL-5-S (human)
(amino acid sequence; vaccine compns. comprising mol. antigen array against cancer, infection, and allergy)

IT 444041-57-0 444041-59-2 444041-61-6 444041-64-9 444041-67-2
444041-81-0 444041-96-7 444042-17-5 444042-18-6 444042-19-7
444042-20-0 444042-21-1 444042-22-2 444042-23-3 444042-24-4
444042-25-5 444042-26-6 444042-27-7 444042-28-8 444042-29-9
444042-30-2 444042-31-3 444042-32-4 444042-33-5 444042-34-6
444042-35-7 444042-36-8 444042-37-9 444042-38-0 444042-39-1
444042-40-4 444042-41-5 444042-42-6 444042-43-7 444042-44-8
444042-45-9 444042-47-1 444042-48-2 444042-49-3 444042-50-6
444042-51-7 444042-52-8 444042-53-9 444042-54-0 444042-55-1
444042-61-9 444042-62-0 444042-69-7 444042-71-1 444042-72-2
444042-73-3 444042-74-4 444042-75-5 444042-76-6 444042-77-7
444042-98-2 444043-18-9 444043-19-0 **444043-20-3**
444043-25-8 444043-26-9 444141-51-9
(unclaimed protein sequence; vaccine compns. comprising mol. antigen array against cancer, infection, and allergy)

L16 ANSWER 10 OF 22 USPATFULL on STN
AN 2003:244219 USPATFULL
TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE (non-U.S. corporation)
PI US 2003170628 A1 20030911
AI US 2001-999570 A1 20011114 (9)
RLI Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING
PRAI WO 2001-IB1715 20010806
US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)
DT Utility
FS APPLICATION
LREP SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, 2421 N.W. 41ST STREET, SUITE A-1, GAINESVILLE, FL, 326066669
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0547] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL,

chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.

DETD [1027] In a further embodiment, the present protein provides a method to purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.

DETD [1215] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amylcidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein.

DETD [1385] The cDNA of Clone 646477.sub.--181-19-2-0-F4-F (SEQ ID NO:105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO:106, comprising the amino acid sequence:

DETD [1387] The protein of SEQ ID NO:106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession numberP02749). Like apoliprotein H, the protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi 3), amino acids 205 to 260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO:106, is highly

expressed in liver.

DETD [1388] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOH) may prevent activation of the intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell-humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase activity of platelets. NAPOH exerts multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1389] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO: 106.

DETD [1763] Antibody preparations prepared according to either the monoclonal or the polyclonal protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

TABLE I

SEQ ID NO.	Sequence Type	Clone ID_Clone Name	ATCC Name	ATCC Deposit	Deposit Date
1	DNA	223583_114-044-2-0-E11-F	S-100A10rP	PTA-2732	Nov. 27, 2000
2	Protein	223583_114-044-2-0-E11-F	S-100A10rP	PTA-2732	Nov. 27, 2000
3	DNA	1000848582_181-40-4-0-A11-F	SCPhx	PTA-2732	Nov. 27, 2000
4	Protein	1000848582_181-40-4-0-A11-F	SCPhx	PTA-2732	Nov. 27, 2000

5	DNA	1000839315_220-26-1-0-F3-F	Chimerin	PTA-2732
	Nov. 27, 2000			
6	Protein	1000839315_220-26-1-0-F3-F	Chimerin	PTA-2732
	Nov. 27, 2000			
7	DNA	1000770704_208-27-3-0-G6-F	CalX	PTA-2732
	Nov. 27, 2000			
8	Protein	1000770704_208-27-3-0-G6-F	CalX	PTA-2732
	Nov. 27, 2000			
9	DNA	147103_106-024-1-0-H6-F	sLRP10	PTA-2534
	Sep. 27, 2000			
10	Protein	147103_106-024-1-0-H6-F	sLRP10	PTA-2534
	Sep. 27, 2000			
11	DNA	224168_116-096-3-0-G11-F	sLRP10	PTA-2534
	Sep. 27, 2000			
12	Protein	224168_116-096-3-0-G11-F	sLRP10	PTA-2534
	Sep. 27, 2000			
13	DNA	243303_116-118-4-0-A3-F	sLRP10	PTA-2534
	Sep. 27, 2000			
14	Protein	243303_116-118-4-0-A3-F	sLRP10	PTA-2534
	Sep. 27, 2000			
15	DNA	225432_116-083-3-0-C6-F	sLRP10	PTA-2534
	Sep. 27, 2000			
16	Protein	225432_116-083-3-0-C6-F	sLRP10	PTA-2534
	Sep. 27, 2000			
17	DNA	229633_114-049-1-0-D3-F	STAMSAP	PTA-2534
	Sep. 27, 2000			
18	Protein	229633_114-049-1-0-D3-F	STAMSAP	PTA-2534
	Sep. 27, 2000			
19	DNA	158523_106-030-2-0-A3-F	OAR	PTA-2732
	Nov. 27, 2000			
20	Protein	158523_106-030-2-0-A3-F	OAR	PTA-2732
	Nov. 27, 2000			
21	DNA	589198_184-11-1-0-E4-F	COVI	PTA-2732
	Nov. 27, 2000			
22	Protein	589198_184-11-1-0-E4-F	COVI	PTA-2732
	Nov. 27, 2000			
23	DNA	47-14-1-C3-CL0 5	APIP	98921
	Oct. 15, 1998			
24	Protein	47-14-1-C3-CL0 5	APIP	98921
	Oct. 15, 1998			
25	DNA	545542_182-1-2-0-D12-F	FGF-22	PTA-2534
	Sep. 27, 2000			
26	Protein	545542_182-1-2-0-D12-F	FGF-22	PTA-2534
	Sep. 27, 2000			
27	DNA	117401_106-006-4-0-B11-F	Frangiopogen	PTA-2534
	Sep. 27, 2000			
28	Protein	117401_106-006-4-0-B11-F	Frangiopogen	PTA-2534
	Sep. 27, 2000			
29	DNA	133431_105-092-4-0-G11-F	Armapoptin	PTA-2534
	Sep. 27, 2000			
30	Protein	133431_105-092-4-0-G11-F	Armapoptin	PTA-2534
	Sep. 27, 2000			
31	DNA	477709_174-8-2-0-C10-F	Pretactilin	PTA-2534
	Sep. 27, 2000			
32	Protein	477709_174-8-2-0-C10-F	Pretactilin	PTA-2534
	Sep. 27, 2000			
33	DNA	145606_106-023-2-0-B3-F	MS4A5	PTA-2534
	Sep. 27, 2000			
34	Protein	145606_106-023-2-0-B3-F	MS4A5	PTA-2534
	Sep. 27, 2000			
35	DNA	1000769575_208-22-1-0-B2-F	Antaginin	PTA-2732
	Nov. 27, 2000			
36	Protein	1000769575_208-22-1-0-B2-F	Antaginin	PTA-2732
	Nov. 27, 2000			

37	DNA	146994_106-023-4-0-C9-F	Beferin	PTA-2732
	Nov. 27, 2000			
38	Protein	146994_106-023-4-0-C9-F	Beferin	PTA-2732
	Nov. 27, 2000			
39	DNA	1000838788_228-28-4-0-F7-F	RP	PTA-2732
	Nov. 27, 2000			
40	Protein	1000838788_228-28-4-0-F7-F	RP	PTA-2732
	Nov. 27, 2000			
41	DNA	1000943975_160-213-2-0-A5-F	SSSPI	PTA-2732
	Nov. 27, 2000			
42	Protein	1000943975_160-213-2-0-A5-F	SSSPI	PTA-2732
	Nov. 27, 2000			
43	DNA	147441_106-025-2-0-C11-F	CPI-1	
44	Protein	147441_106-025-2-0-C11-F	CPI-1	
45	DNA	124610_113-003-3-0-HS-F	RET-A-MODULIN	PTA-2732
	Nov. 27, 2000			
46	Protein	124610_113-003-3-0-HS-F	RET-A-MODULIN	PTA-2732
	Nov. 27, 2000			
47	DNA	1000855165_205-99-1-0-A5-F	Tifapinix	PTA-2732
	Nov. 27, 2000			
48	Protein	1000855165_205-99-1-0-A5-F	Tifapinix	PTA-2732
	Nov. 27, 2000			
49	DNA	588098_184-11-4-0-H4-F	CrypAAT	PTA-2732
	Nov. 27, 2000			
50	Protein	588098_184-11-4-0-H4-F	CrypAAT	PTA-2732
	Nov. 27, 2000			
51	DNA	500721700_204-43-4-0-H10-F	Tifapinix-A58S	
52	Protein	500721700_204-43-4-0-H10-F	Tifapinix-A58S	
53	DNA	789749_182-14-3-0-C12-F	Plasminute	PTA-2732
	Nov. 27, 2000			
54	Protein	789749_182-14-3-0-C12-F	Plasminute	PTA-2732
	Nov. 27, 2000			
55	DNA	519757_184-4-2-0-F7-F	CALSIGN	PTA-2732
	Nov. 27, 2000			
56	Protein	519757_184-4-2-0-F7-F	CALSIGN	PTA-2732
	Nov. 27, 2000			
57	DNA	625004_188-15-4-0-H6-F	vCOL16A1	PTA-2534
	Sep. 27, 2000			
58	Protein	625004_188-15-4-0-H6-F	vCOL16A1	PTA-2534
	Sep. 27, 2000			
59	DNA	422353_145-11-3-0-E7-F	NKS	PTA-2534
	Sep. 27, 2000			
60	Protein	422353_145-11-3-0-E7-F	NKS	PTA-2534
	Sep. 27, 2000			
61	DNA	500715621_204-15-3-0-C6-F	PLasminogen Carrier Protein (PLCP)	PTA-2534
	Sep. 27, 2000			
62	Protein	500715621_204-15-3-0-C6-F	PLasminogen Carrier Protein (PLCP)	PTA-2534
	Sep. 27, 2000			
63	DNA	165843_116-008-4-0-G4-F	Novel Calpastatin 1 (NC1)	PTA-2534
	Sep. 27, 2000			
64	Protein	165843_116-008-4-0-G4-F	Novel	PTA-2534
	Sep. 27, 2000			

			Calpastatin 1 (NC1)	
65	DNA	335752_157-15-4-0-B11-F	Novel Calpastatin 2 (NC2)	
66	Protein	335752_157-15-4-0-B11-F	Novel Calpastatin 2 (NC2)	
67	DNA	646607_181-15-2-0-E2-F	Benzodiazepine Receptor 2 (BZRP-R2)	PTA-2534 Sep. 27, 2000
68	Protein	646607_181-15-2-0-E2-F	Benzodiazepine Receptor 2 (BZRP-R2)	PTA-2534 Sep. 27, 2000
69	DNA	229654_114-049-1-0-F12-F	LAP	
70	Protein	229654_114-049-1-0-F12-F	LAP	
71	DNA	338116_174-1-1-0-B10-F	Short Histone Deacetylase (SHDAC)	PTA-2534 Sep. 27, 2000
72	Protein	338116_174-1-1-0-B10-F	Short Histone Deacetylase (SHDAC)	PTA-2534 Sep. 27, 2000
73	DNA	500716683_204-24-2-0-D12-F	Protease-associated Paraplegin (PAP)	PTA-2534 Sep. 27, 2000
74	Protein	500716683_204-24-2-0-D12-F	Protease-associated Paraplegin (PAP)	PTA-2534 Sep. 27, 2000
75	DNA	500760207_205-58-4-0-H6-F	Ketothiolase (KT)	
76	Protein	500760207_205-584-0-H6-F	Ketothiolase (KT)	
77	DNA	122421_105-076-4-0-H1-F	BASI2	
78	Protein	122421_105-076-4-0-H1-F	BASI2	
79	DNA	99483_105-016-1-0-D7-F	KSPI1	PTA-2534 Sep. 27, 2000
80	Protein	99483_105-016-1-0-D7-F	KSPI1	PTA-2534 Sep. 27, 2000
81	DNA	517778_184-5-3-0-G3-F	Amyloid Apoptotic Receptor (AAR)	
82	Protein	517778_184-5-3-0-G3-F	Amyloid Apoptotic Receptor (AAR)	
83	DNA	100038_105-017-4-0-E4-F	Soluble Activator of Wnt 1 (SAW-1)	
84	Protein	100038_105-017-4-0-E4-F	Soluble Activator of Wnt 1 (SAW-1)	

85	DNA	100523_105-019-1-0-F3-F	Soluble Activator of Wnt 1 (SAW-1)	
86	Protein	100523_105-019-1-0-F3-F	Soluble Activator of Wnt 1 (SAW-1)	
87	DNA	116470_105-063-3-0-H7-F	Dopamine AMPhetamine INhibitor (Dampin)	
88	Protein	116470_105-063-3-0-H7-F	Dopamine AMPhetamine INhibitor (Dampin)	
89	DNA	122600_105-077-3-0-F9-F	Dopamine AMPhetamine INhibitor (Dampin)	PTA-2732 Nov. 27, 2000
90	Protein	122600_105-077-3-0-F9-F	Dopamine AMPhetamine INhibitor (Dampin)	PTA-2732 Nov. 27, 2000
91	DNA	651658_181-35-2-0-C8-F	VAGS	
92	Protein	651658_181-35-2-0-C8-F	VAGS	
93	DNA	150011_110-006-3-0-D5-F	TFPI-C16Pfs	
94	Protein	150011_110-006-3-0-D5-F	TFPI-C16Pfs	
95	DNA	500737461_205-43-3-0-E3-F	TFPI-M162Qfs	
96	Protein	500737461_205-43-3-0-E3-F	TFPI-M162Qfs	
97	DNA	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
98	Protein	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
99	DNA	479155_174-4-4-0-C8-F	ADEVAR	PTA-2732 Nov. 27, 2000
100	Protein	479155_174-4-4-0-C8-F	ADEVAR	PTA-2732 Nov. 27, 2000
101	DNA	586587_181-9-2-0-CS-F	ATP-binding cassette 1, hABC	
102	Protein	586587_181-9-2-0-C5-F	ATP-binding cassette, hABC	
103	DNA	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534 Sep. 27, 2000
104	Protein	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534 Sep. 27, 2000
105	DNA	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
106	Protein	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
107	DNA	113165_105-056-3-0-G12-F	human JNK3-binding	

			protein (hJNK3-BP)
108	Protein	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)
109	DNA	231462_117-065-1-0-G11-F	DROCK2
110	Protein	231462_117-065-1-0-G11-F	DROCK2
111	DNA	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)
112	Protein	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
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(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 11 OF 22 USPATFULL on STN
AN 2003:231986 USPATFULL
TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE (non-U.S. corporation)
PI US 2003162186 A1 20030828
AI US 2002-154678 A1 20020522 (10)
PRAI US 2001-293574P 20010525 (60)
US 2001-298698P 20010615 (60)
US 2001-302277P 20010629 (60)
US 2001-305456P 20010713 (60)
DT Utility
FS APPLICATION
LREP SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, 2421 N.W. 41ST STREET, SUITE A-1, GAINESVILLE, FL, 326066669
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0546] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL, chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid

matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.

DETD [1014] In a further embodiment, the present protein provides a method to purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.

DETD [1188] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amyloidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein.

DETD [1350] The cDNA of Clone 646477.sub.--181-19-2-0-F4-F (SEQ ID NO:105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO:106, comprising the amino acid sequence: MISPVLILFSSFLCHVAIAGRTCPKPDDLPFSTVVP LKTFYEPGEEITYSCKPGYVSRGGMRK FICPLTGLWLINTLKCTPRVCPFAGILENGAVRYTTFEYPNTIS FSCNTGFYLNGADSAKCT EEGKWSPELPVCAPHCPPPSIPTFATLRVYKPSAGNNSLYRDTAVFECLPQHA MFGNDTIT CTTHGNWTKLPECREVKCPFPSRPDNGFVNYPAKPTLYYKDKATFGCHDGYSLDGPEEIE CTKLGNWSAMPSCKASCKVPVKKATVVYQGERVKIQEKFKNGMLHGDKVSFFCKNKEK KCSYTEDAQCIDGTIEVPKCFKEHSSLAFWKTDASDVKPC. Accordingly, it will be appreciated that all characteristics and uses of the polypeptides of SEQ ID NO:106 described throughout the present application also pertain to the polypeptides encoded by the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. In addition, it will be appreciated that all characteristics and uses of the polynucleotides of SEQ ID NO:105 described throughout the present application also pertain to the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. A preferred embodiment of the invention is directed toward the compositions of SEQ ID NO:105, SEQ ID NO:106, and Clone 646477.sub.--181-19-2-0-F4-F. Also preferred are polypeptide fragments having a biological activity as described herein and the polynucleotides encoding the fragments.

DETD [1351] The protein of SEQ ID NO:106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession numberP02749). Like apoliprotein H, the

protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi 3), amino acids 205 to 260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO:106, is highly expressed in liver.

DETD [1352] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOH) may prevent activation of the intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell-humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase acitvity of platelets. NAPOH exerts multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1353] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO: 106.

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 12 OF 22 USPATFULL on STN
AN 2003:225673 USPATFULL

TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE (non-U.S. corporation)
PI US 2003157485 A1 20030821
AI US 2001-992095 A1 20011113 (9)
RLI Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING
PRAI WO 2001-IB1715 20010806
US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)
DT Utility
FS APPLICATION
LREP SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, 2421 N.W. 41ST STREET, SUITE A-1, GAINESVILLE, FL, 326066669
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25484
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0534] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL, chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.
DETD [0986] In a further embodiment, the present protein provides a method to purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.
DETD [1150] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amyloidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in

carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein.

DETD [1303] The cDNA of Clone 646477.sub.--181-19-2-0-F4-F (SEQ ID NO: 105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO: 106, comprising the amino acid sequence: MISPVLILFSSFLCHVAIAGRTCPKPDDLPFSTVVP LKTFYEPGEEITYSCKPGYVSRGGMRK FICPLTGLWLINTLKCTPRVCPFAGILENGAVRYTTFEYPNTIS FSCNTGFYLNGADSAKCT EEGKWSPELPVCAPIICPPPSIPTFATLRVYKPSAGNNSLYRDTAVFECLPQH AMFGNDTIT CTTHGNWTKLPECREVKCPFPSRPDNGFVNYPAKPTLYYKDKATFGCHDGYSLDGPEEIE CTKLGNWSAMPSCKASCKVPVKKATVVYQGERVKIQEKFKNGMLHGDKVSFFCKNKEK KCSYTEDAQCIDGTIEVPKCFKEHSSLAFWKTDASDVKPC. Accordingly, it will be appreciated that all characteristics and uses of the polypeptides of SEQ ID NO: 106 described throughout the present application also pertain to the polypeptides encoded by the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. In addition, it will be appreciated that all characteristics and uses of the polynucleotides of SEQ ID NO: 105 described throughout the present application also pertain to the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. A preferred embodiment of the invention is directed toward the compositions of SEQ ID NO: 105, SEQ ID NO: 106, and Clone 646477.sub.--181-19-2-0-F4-F. Also preferred are polypeptide fragments having a biological activity as described herein and the polynucleotides encoding the fragments.

DETD [1304] The protein of SEQ ID NO: 106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession numberP02749). Like apoliprotein H, the protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi 3), amino acids 205 to 260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO: 106, is highly expressed in liver.

DETD [1305] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOH) may prevent activation of the intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell-humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase acitvity of platelets. NAPOH exerts multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid

autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1306] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO: 106.

DETD [1677] Antibody preparations prepared according to either the monoclonal or the polyclonal protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

TABLE I

SEQ ID NO.	Sequence Type	Clone ID_Clone Name	Name	ATCC Deposit	ATCC Deposit Date
1	DNA	223583_114-044-2-0-E11-F	S-100A10rP	PTA-2732	Nov. 27, 2000
2	Protein	223583_114-044-2-0-E11-F	S-100A10rP	PTA-2732	Nov. 27, 2000
3	DNA	1000848582_181-40-4-0-A11-F	SCPhx	PTA-2732	Nov. 27, 2000
4	Protein	1000848582_181-40-4-0-A11-F	SCPhx	PTA-2732	Nov. 27, 2000
5	DNA	1000839315_220-26-1-0-F3-F	Chimerin	PTA-2732	Nov. 27, 2000
6	Protein	1000839315_220-26-1-0-F3-F	Chimerin	PTA-2732	Nov. 27, 2000
7	DNA	1000770704_208-27-3-0-G6-F	CalX	PTA-2732	Nov. 27, 2000
8	Protein	1000770704_208-27-3-0-G6-F	CalX	PTA-2732	Nov. 27, 2000
9	DNA	147103_106-024-1-0-H6-F	sLRP10	PTA-2534	Sep. 27, 2000
10	Protein	147103_106-024-1-0-H6-F	sLRP10	PTA-2534	Sep. 27, 2000
11	DNA	224168_116-096-3-0-G11-F	sLRP10	PTA-2534	Sep. 27, 2000
12	Protein	224168_116-096-3-0-G11-F	sLRP10	PTA-2534	Sep. 27, 2000

87	DNA	116470_105-063-3-0-H7-F	Dopamine AMPhetamine INhibitor (Dampin)	
88	Protein	116470_105-063-3-0-H7-F	Dopamine AMPhetamine INhibitor (Dampin)	
89	DNA Nov. 27, 2000	122600_105-077-3-0-F9-F	Dopamine AMPhetamine INhibitor (Dampin)	PTA-2732
90	Protein Nov. 27, 2000	122600_105-077-3-0-F9-F	Dopamine AMPhetamine INhibitor (Dampin)	PTA-2732
91	DNA	651658_181-35-2-0-C8-F	VAGS	
92	Protein	651658_181-35-2-0-C8-F	VAGS	
93	DNA	150011_110-006-3-0-D5-F	TFPI-C16Pfs	
94	Protein	150011_110-006-3-0-D5-F	TFPI-C16Pfs	
95	DNA	500737461_205-43-3-0-E3-F	TFPI-M162Qfs	
96	Protein	500737461_205-43-3-0-E3-F	TFPI-M162Qfs	
97	DNA	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
98	Protein	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
99	DNA Nov. 27, 2000	479155_174-4-4-0-C8-F	ADEVAR	PTA-2732
100	Protein PTA-2732	479155_174-4-4-0-C8-F Nov. 27, 2000	**ADEVAR**	
101	DNA	586587_181-9-2-0-C5-F	ATP-binding cassette 1, hABC	
102	Protein	586587_181-9-2-0-C5-F	ATP-binding cassette, hABC	
103	DNA Sep. 27, 2000	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534
104	Protein Sep. 27, 2000	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534
105	DNA	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
106	Protein	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
107	DNA	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)	
108	Protein	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)	
109	DNA	231462_117-065-1-0-G11-F	DROCK2	
110	Protein	231462_117-065-1-0-G11-F	DROCK2	

111	DNA	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)
112	Protein	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 13 OF 22 USPATFULL on STN
AN 2003:140406 USPATFULL
TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)
PI US 2003096247 A1 20030522
AI US 2001-986 A1 20011114 (10)
RLI Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING
PRAI WO 2001-IB1715 20010806
US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)
DT Utility
FS APPLICATION
LREP John Lucas, Ph.D., J.D., GENSET CORP., 10665 Sorrento Valley Road, San Diego, CA, 92121-1609
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25656
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0547] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL, chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.
DETD [1031] In a further embodiment, the present protein provides a method to

purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.

DETD [1227] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amyloidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein. In a preferred embodiment of the invention, a ligand-binding polypeptide fragment of AAR is used to prevent cell death. This method comprises the step of: contacting a ligand-binding fragment of AAR with ligand in an amount effective to competitively inhibit binding of ligand to AAR expressed on a cell. Preferred polypeptide fragments of AAR include but are not limited to those starting at an amino acid chosen from amino acids 1-40 and ending at an amino acid chosen from amino acids 165-180. Any single AAR fragment or combination of AAR fragments included in said list may be excluded from this embodiment of the invention. The most preferred fragment comprises amino acids 1-180 of AAR. Preferred forms of inhibited cell death include those associated with amyloidgenic peptides, such as pancreatic K-islet cell death and others listed herein. AAR fragments may be applied by methods common to the art such as those discussed herein. For example, AAR fragments may be delivered to cells of the pancreas in physiologically acceptable form by direct injection or catheter. For prolonged treatment, AAR fragments may be released from an implantable polypeptide-releasing stent (U.S. Pat. No. 5,683,345 and U.S. Pat. No. 5,500,013, which disclosures are hereby incorporated by reference in their entireties).

DETD [1401] The cDNA of Clone 646477.sub.--181-19-2-0-F4-F (SEQ ID NO:105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO: 106, comprising the amino acid sequence:

DETD [1403] The protein of SEQ ID NO: 106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession number P02749). Like apoliprotein H, the protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi 3), amino acids 205 to

260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO:106, is highly expressed in liver.

DETD [1404] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOH) may prevent activation of the intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell-humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase activity of platelets. NAPOH exerts multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1405] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO: 106.

DETD [1775] Antibody preparations prepared according to either the monoclonal or the polyclonal protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

TABLE I

SEQ ID NO.	Sequence Type	Clone ID_Clone Name	Name	ATCC Deposit ATCC Deposit Date
1	DNA	223583_114-044-2-0-E11-F	S-100A10rP	

106	Protein	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)
107	DNA	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)
108	Protein	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)
109	DNA	231462_117-065-1-0-G11-F	DROCK2
110	Protein	231462_117-065-1-0-G11-F	DROCK2
111	DNA	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)
112	Protein	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 14 OF 22 USPATFULL on STN
AN 2003:133926 USPATFULL
TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)
PI US 2003092011 A1 20030515
AI US 2001-489 A1 20011114 (10)
RLI Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING
PRAI WO 2001-IB1715 20010806
US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)
DT Utility
FS APPLICATION
LREP John Lucas, Ph.D., J.D., GENSET CORP., 10665 Sorrento Valley Road, San Diego, CA, 92121-1609
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25607
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0544] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical

field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL, chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.

DETD [0995] In a further embodiment, the present protein provides a method to purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.

DETD [1161] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amyloidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein.

DETD [1319] The cDNA of Clone 646477.sub.--181-19-2-0-F4-F (SEQ ID NO:105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO:106, comprising the amino acid sequence: MISPVLILFSSFLCHVAIAGRTCPKPDDLPFSTVVP LKTFYEPGEEITYSCKPGYVSRGGMRK FICPLTGLWLINTLKCTPRVCPFAGILENGAVRYTTFEYPNTIS FSCNTGFYLNGADSAKCT EEGKWSPELPVCAPIICPPPSIPTFATLRVYKPSAGNNSLYRDTAVFECLPQH AMFGNDTIT CTTHGNWTKLPECREVKCPFPSRPDNGFVNYPAKPTLYYKDKATFGCHDGYSLDGPEEIE CTKLGNWSAMPSCKASCKVPVKKATVVYQGERVKIQEKFKNGMLHGDKVSFFCKNKEK KCSYTEDAQCIDGTIEVPKCFKEHSSLAFWKTDASDVKPC. Accordingly, it will be appreciated that all characteristics and uses of the polypeptides of SEQ ID NO:106 described throughout the present application also pertain to the polypeptides encoded by the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. In addition, it will be appreciated that all characteristics and uses of the polynucleotides of SEQ ID NO:105 described throughout the present application also pertain to the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. A preferred

embodiment of the invention is directed toward the compositions of SEQ ID NO:105, SEQ ID NO:106, and Clone 646477.sub.--181-19-2-0-F4-F. Also preferred are polypeptide fragments having a biological activity as described herein and the polynucleotides encoding the fragments.

DETD [1320] The protein of SEQ ID NO:106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession numberP02749). Like apoliprotein H, the protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi 3), amino acids 205 to 260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO:106, is highly expressed in liver.

DETD [1321] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOH) may prevent activation of the intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell-humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase acitvity of platelets. NAPOH exerts multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1322] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO:106.

DETD [1692] Antibody preparations prepared according to either the monoclonal or the polyclonal protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

TABLE I

			M162Qfs	
97	DNA	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
98	Protein	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
99	DNA	479155_174-4-4-0-C8-F	ADEVAR	PTA-2732
	Nov. 27, 2000			
100	Protein	479155_174-4-4-0-C8-F	**ADEVAR**	
	PTA-2732	Nov. 27, 2000		
101	DNA	586587_181-9-2-0-C5-F	ATP-binding cassette 1, hABC	
102	Protein	586587_181-9-2-0-C5-F	ATP-binding cassette, hABC	
103	DNA	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534
	Sep. 27, 2000			
104	Protein	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534
	Sep. 27, 2000			
105	DNA	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
106	Protein	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
107	DNA	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)	
108	Protein	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)	
109	DNA	231462_117-065-1-0-G11-F	DROCK2	
110	Protein	231462_117-065-1-0-G11-F	DROCK2	
111	DNA	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)	
112	Protein	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)	

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 15 OF 22 USPATFULL on STN

AN 2003:37603 USPATFULL
TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)
PI US 2003027248 A1 20030206
AI US 2001-924340 A1 20010806 (9)
PRAI US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)
DT Utility
FS APPLICATION
LREP GENSET, JOHN LUCAS, PHD, J.D., 10665 SORRENTO VALLEY RD, SAN DIEGO, CA, 92121
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25650
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0464] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL, chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP 10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.
DETD [0924] In a further embodiment, the present protein provides a method to purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.
DETD [1099] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amyloidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic

bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic. .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein.

DETD [1263] The cDNA of Clone 646477.sub.--181-19-2-0-F4-F (SEQ ID NO:105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO:106, comprising the amino acid sequence:

DETD [1265] The protein of SEQ ID NO:106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession numberP02749). Like apoliprotein H, the protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi amino acids 205 to 260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO:106, is highly expressed in liver.

DETD [1266] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOH) may prevent activation of the intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell-humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase acitvity of platelets. NAPOH exerts multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1267] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO:106.

DETD [1599] Antibody preparations prepared according to either the monoclonal

			(Dampin)	
91	DNA	651658_181-35-2-0-C8-F	VAGS	
92	Protein	651658_181-35-2-0-C8-F	VAGS	
93	DNA	150011_110-006-3-0-DS-F	TFPI-C16Pfs	
94	Protein	150011_110-006-3-0-DS-F	TFPI-C16Pfs	
95	DNA	500737461_205-43-3-0-E3-F	TFPI-M162Qfs	
96	Protein	500737461_205-43-3-0-E3-F	TFPI-M162Qfs	
97	DNA	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
98	Protein	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2 (SAW-2)	
99	DNA	479155_174-4-4-0-C8-F	ADEVAR	PTA-2732
	Nov. 27, 2000			
100	Protein	479155_174-4-4-0-C8-F	**ADEVAR**	
	PTA-2732	Nov. 27, 2000		
101	DNA	586587_181-9-2-0-C5-F	ATP-binding cassette 1, hABC	
102	Protein	586587_181-9-2-0-C5-F	ATP-binding cassette, hABC	
103	DNA	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534
	Sep. 27, 2000			
104	Protein	620315_188-13-1-0-G12-F	MOBP-81h	PTA-2534
	Sep. 27, 2000			
105	DNA	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
106	Protein	646477_181-19-2-0-F4-F	novel Apolipoprotein H (NAPOH)	
107	DNA	113165_105-056-3-0-G12-F	human JNK3-binding protein (hJNK3-BP)	
108	Protein	113165_105-056-3-0-G12-F	human JNK3-binding protein (hThK3-BP)	
109	DNA	231462_117-065-1-0-G11-F	DROCK2	
110	Protein	231462_117-065-1-0-G11-F	DROCK2	
111	DNA	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)	
112	Protein	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid dehydrogenase type 2 (NBHSD2)	

IT	477744-37-9P	477744-39-1P	477744-41-5P	477744-43-7P	477744-45-9P
	477744-50-6P	477744-52-8P	477744-54-0P	477744-56-2P	477744-58-4P
	477744-60-8P	477744-62-0P	477744-64-2P	477744-66-4P	477744-68-6P
	477744-70-0P	477744-72-2P	477744-74-4P	477744-76-6P	477744-78-8P
	477744-80-2P	477744-82-4P	477744-84-6P	477744-86-8P	477744-88-0P
	477744-90-4P	477744-92-6P	**477744-94-8P**	477744-96-0P	
	477744-98-2P	477745-00-9P	477745-02-1P	477745-04-3P	477745-06-5P

477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 16 OF 22 USPATFULL on STN
AN 2003:37516 USPATFULL
TI Human cDNAs and proteins and uses thereof
IN Bejanin, Stephane, Paris, FRANCE
Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)
PI US 2003027161 A1 20030206
AI US 2001-992600 A1 20011113 (9)
RLI Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING
PRAI WO 2001-IB1715 20010806
US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)
DT Utility
FS APPLICATION
LREP John Lucas, Ph.D., J.D., GENSET CORP., 10665 Sorrento Valley Road, San Diego, CA, 92121-1609
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 25529
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0547] High levels of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), chylomicrons, and **Apolipoprotein** E (ApoE) are associated with atherosclerosis and other cholesterol-associated disorders. These molecules are subjects of intense study in the medical field. As a preferred embodiment, sLRP10 is used to bind LDL, VLDL, chylomicrons, and ApoE. While many members of the LDLR family, such as LDLR and alpha-2-macroglobulin receptor, are very large (>400 kD) membrane spanning proteins, sLRP10 is relatively small and not membrane associated. Thus, sLRP10 is an easily purified polypeptide that can be used for binding LDLR domain ligands. As a part of this embodiment, sLRP10 polypeptide is covalently or non-covalently attached to a solid matrix and allowed to bind LDL, VLDL, chylomicrons, or ApoE in solution using techniques well known in the art. Once bound, these proteins can be purified using the following steps: i) wash the solid matrix to get rid of contaminants, ii) elute the protein of interest using more stringent conditions, e.g., increasing salt concentration.
DETD [0994] In a further embodiment, the present protein provides a method to purify a protein harboring one or more kringle domains from a cellular extract, the method comprising using a fragment of the present protein retaining an intact CRD domain, preferably a fragment restricted to the CRD domain itself, to purify the kringle domain-containing protein, e.g. using a method such as affinity chromatography. Preferably, the protein to be purified is selected from the group consisting of plasminogen, angiostatin, thrombin, Hepatocyte Growth Factor, Macrophage Stimulating Protein and **apolipoprotein** a. The protein to be purified using the present method is derived from any source, e.g. protein expressed in vitro using an invertebrate, yeast or bacterial heterologous expression system.
DETD [1153] The amino-terminus of AAR is capable of binding to ligands such as amyloidgenic peptides (i.e., the .beta.-amyloid peptide associated with Alzheimer's disease, Amyloid Precursor Like Proteins (APLP) 1 and 2, immunoglobulin light chain, prealbumin, .beta.-2-microglobulin, transthyretin, amylin, insulin, atrial natriuretic peptide (ANP), **apolipoproteins** and glucagon). The amyloidgenic fragments of

these proteins form predominantly beta-pleated sheet structures that may adopt the fibrillar configuration of amyloid in certain pathologic states. Amyloid deposits often lead to cell death in affected tissues. Amyloid-associated disorders include, most notably, Alzheimer's disease, diabetes, systemic amyloidosis, familial visceral amyloidosis, cutaneous amyloidosis, Muckle-Wells syndrome, Gerstman-Straussler disease, dialysis-related and hemodialysis-related amyloidosis. Amyloid deposits may lead to further pathogenic outcomes depending on the affected tissue. For instance, hemodialysis-related amyloidosis can result in carpal tunnel syndrome, erosive arthropathy, spondyloarthropathy, lytic bone lesions, and pathologic fractures. .beta.-amyloid peptide deposition in the tunica media of leptomeningeal and parenchymal vessels causes degradation of smooth muscle cells and subsequent cortical hemorrhages. Furthermore, the neuronal cell death observed in Alzheimer's disease is associated with the senility that accompanies the later stages of the disease and pancreatic .beta.-islet cell death is a causative factor of disrupted insulin regulation in diabetes. Reducing the level of amyloidgenic peptides is a desired therapy for disorders such as those listed herein.

DETD [1309] The cDNA of Clone 646477 181-19-2-0-F4-F (SEQ ID NO:105) **encodes** novel Apolipoprotein H (NAPOH) of SEQ ID NO:106, comprising the amino acid sequence: MISPVLILFSSFLCHVAIAGRTCPKPDDLPFSTVVP LKTFYEPGEEITYSCKPGYVSRGGMRK FICPLTGLWLINTLKCTPRVCPFAGILENGAVRYTTFEYPNTIS FSCNTGFYLNGADSAKCT EEGKWSPELPVCAPIICPPPSIPTFATLRVYKPSAGNNSLYRDTAVFECLPQH AMFGNDTIT CTTHGNWTKLPECREVKCPFPSRPDNGFVNYPAKPTLYYKDKATFGCHDGYSLDGPEEIE CTKLGNWSAMPSCKASCKVPVKKATVVYQGERVKIQEKFKNGMLHGDKVSFFCKNKEK KCSYTEDAQCIDGTIEVPKCFKEHSSLAFWKTDASDVKPC. Accordingly, it will be appreciated that all characteristics and uses of the polypeptides of SEQ ID NO:106 described throughout the present application also pertain to the polypeptides encoded by the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. In addition, it will be appreciated that all characteristics and uses of the polynucleotides of SEQ ID NO:105 described throughout the present application also pertain to the nucleic acids included in Clone 646477.sub.--181-19-2-0-F4-F. A preferred embodiment of the invention is directed toward the compositions of SEQ ID NO:105, SEQ ID NO:106, and Clone 646477.sub.--181-19-2-0-F4-F. Also preferred are polypeptide fragments having a biological activity as described herein and the polynucleotides encoding the fragments.

DETD [1310] The protein of SEQ ID NO:106 is a polymorphic variant of the sequence of **apolipoprotein** H or beta-2-glycoprotein I precursor (swissprot accession numberPO2749). Like apoliprotein H, the protein of the invention displays 4 Sushi domains (PF00084) and one sushi-like domain, from amino acids 23 to 79 (Sushi 1), amino acids 84 to 137 (Sushi 2), amino acids 142 to 200 (Sushi 3), amino acids 205 to 260 (Sushi 4) and amino acids 263 to 345 (Sushi-like). Sushi domains are also known as Complement control protein (CCP) modules, or short consensus repeats (SCR), exist in a wide variety of complement and adhesion proteins. Also, it has been reported that the domain V (sushi-like domain) specifically interacts with hydrophobic ligands (Hong, D. P. et al., Biochemistry 40:8092-8100 (2001)). Novel **apolipoprotein** H, the protein of SEQ ID NO:106, is highly expressed in liver.

DETD [1311] Novel **apolipoprotein** H is a plasma protein with the ability to bind with various kinds of negatively charged substances. Novel **apolipoprotein** H (NAPOII) may prevent activation of the intrinsic blood coagulation cascade by binding to phospholipids on the surface of damaged cells. NAPOH is a strong auto-antigen that stimulates a vigorous B cell -humoral response and T cell immunity response. NAPOH has been implicated in a variety of physiologic pathways including lipoprotein metabolism, artherosclerosis and in the production of antiphospholipid autoantibodies ("aPA"). NAPOH also binds to platelets, mitochondria, heparin, DNA, and anionic phospholipids, and has been shown to be involved in the blood coagulation pathway, platelet aggregation, and prothrombinase acitvity of platelets. NAPOH exerts

multiple inhibitory effects on the coagulation pathway and platelet aggregation. NAPOH is considered to be a required cofactor for anionic phospholipids antigen by the aPA found in sera of many patients with chronic inflammatory disease, like systemic lupus erythematosus, and primary antiphospholipid syndrome, but it does not seem to be required for the reactivity of aPA associated with infections. These studies suggest that the NAPOH-phospholipid compex forms the antigen to which aPA are directed. Autoantibodies to phospholipid-free NAPOH are present in patients with primary antiphospolipid syndrome. Antiphospholipid autoantibodies are a heterogeneous group of autoantibodies including most commonly a lupus anticoagulant and anticardiolipin antibodies which are directed against negatively charged phospholipids. The presence of antiphospholipid autoantibodies has been associated with recurrent deep vein thrombosis and other thrombotic complications, including pulmonary, renal, and retinal thrombosis, as well as Budd-Chiari syndrome. In addition, antiphospholipid autoantibodies have been associated with arterial thrombosis including cerebral, retinal, and peripheral arteries. Recurrent fetal losses, usually occurring in the second and third trimester, felt to be due in part to thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency and ultimately fetal loss are associated with antiphospholipid autoantibodies.

DETD [1312] An embodiment of the invention is directed to a composition comprising a novel **Apolipoprotein** H (NAPOH) polypeptide sequence of SEQ ID NO:106.

DETD [1677] Antibody preparations prepared according to either the monoclonal or the polyclonal protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

TABLE I

SEQ ID NO.	Sequence ATCC Type Deposit	ATCC Clone ID_Clone Name Deposit Date	Name
1	DNA PTA-2732	223583_114-044-2-0-E11-F Nov. 27, 2000	S-100A10rP
2	Protein PTA-2732	223583_114-044-2-0-E11-F Nov. 27, 2000	S-100A10rP
3	DNA PTA-2732	1000848582_181-40-4-0-A11-F Nov. 27, 2000	SCPhx
4	Protein PTA-2732	1000848582_181-40-4-0-A11-F Nov. 27, 2000	SCPhx
5	DNA PTA-2732	1000839315_220-26-1-0-F3-F Nov. 27, 2000	Chimerin
6	Protein PTA-2732	1000839315_220-26-1-0-F3-F Nov. 27, 2000	Chimerin
7	DNA PTA-2732	1000770704_208-27-3-0-G6-F Nov. 27, 2000	CalX
8	Protein PTA-2732	1000770704_208-27-3-0-G6-F Nov. 27, 2000	CalX
9	DNA PTA-2534	147103_106-024-1-0-H6-F Sep. 27, 2000	sLRP10
10	Protein PTA-2534	147103_106-024-1-0-H6-F Sep. 27, 2000	sLRP10
11	DNA PTA-2534	224168_116-096-3-0-G11-F Sep. 27, 2000	sLRP10

82	Protein (AAR)	517778_184-5-3-0-G3-F	Amyloid Apoptotic Receptor
83	DNA (SAW-1)	100038_105-017-4-0-E4-F	Soluble Activator of Wnt 1
84	Protein (SAW-1)	100038_105-017-4-0-E4-F	Soluble Activator of Wnt 1
85	DNA (SAW-1)	100523_105-019-1-0-F3-F	Soluble Activator of Wnt 1
86	Protein (SAW-1)	100523_105-019-1-0-F3-F	Soluble Activator of Wnt 1
87	DNA INhibitor	116470_105-063-3-0-H7-F (Dampin)	Dopamine AMPhetamine
88	Protein INhibitor	116470_105-063-3-0-H7-F (Dampin)	Dopamine AMPhetamine
89	DNA INhibitor	122600_105-077-3-0-F9-F (Dampin)	Dopamine AMPhetamine PTA-2732 Nov. 27, 2000
90	Protein INhibitor	122600_105-077-3-0-F9-F (Dampin)	Dopamine AMPhetamine PTA-2732 Nov. 27, 2000
91	DNA	651658_181-35-2-0-C8-F	VAGS
92	Protein	651658_181-35-2-0-C8-F	VAGS
93	DNA	150011_110-006-3-0-D5-F	TFPI-C16Pfs
94	Protein	150011_110-006-3-0-D5-F	TFPI-C16Pfs
95	DNA	500737461_205-43-3-0-E3-F	TFPI-M162Qfs
96	Protein	500737461_205-43-3-0-E3-F	TFPI-M162Qfs
97	DNA (SAW-2)	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2
98	Protein (SAW-2)	100545_105-019-2-0-E3-F	Soluble Activator of Wnt 2
99	DNA PTA-2732	479155_174-4-4-0-C8-F Nov. 27, 2000	ADEVAR
100	Protein PTA-2732	479155_174-4-4-0-C8-F Nov. 27, 2000	**ADEVAR**
101	DNA	586587_181-9-2-0-C5-F	ATP-binding cassette 1, hABC
102	Protein	586587_181-9-2-0-C5-F	ATP-binding cassette, hABC
103	DNA PTA-2534	620315_188-13-1-0-G12-F Sep. 27, 2000	MOBP-81h
104	Protein PTA-2534	620315_188-13-1-0-G12-F Sep. 27, 2000	MOBP-81h
105	DNA (NAPOH)	646477_181-19-2-0-F4-F	novel Apolipoprotein H
106	Protein (NAPOH)	646477_181-19-2-0-F4-F	novel Apolipoprotein H
107	DNA (hJNK3-BP)	113165_105-056-3-0-G12-F	human JNK3-binding protein
108	Protein (hJNK3-BP)	113165_105-056-3-0-G12-F	human JNK3-binding protein
109	DNA	231462_117-065-1-0-G11-F	DROCK2
110	Protein	231462_117-065-1-0-G11-F	DROCK2
111	DNA dehydrogenase type 2 (NBHSD2)	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid
112	Protein dehydrogenase type 2 (NBHSD2)	500723589_205-34-3-0-G4-F	Novel 17 beta-hydroxysteroid

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
(amino acid sequence; human cDNAs and proteins and their uses for

screening and diagnostic assays)

L16 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:964539 CAPLUS
DN 138:34222
TI Differentially expressed human genes and their encoded proteins useful for identification, assessment, prevention, and therapy of cervical cancer
IN Schlegel, Robert; Chen, Yan; Zhao, Xumei; Monahan, John E.; Kamatkar, Shubhangi; Gannavarapu, Manjula; Glatt, Karen; Hoersch, Sebastian
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 386 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002101075	A2	20021219	WO 2002-US18638	20020612
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003087270	A1	20030508	US 2002-171311	20020612
PRAI	US 2001-298155P	P	20010613		
	US 2001-298159P	P	20010613		
	US 2001-335936P	P	20011114		

IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(L-1; differentially expressed human genes and their encoded proteins useful for identification, assessment, prevention, and therapy of cervical cancer)

IT 478622-90-1 478737-00-7 478737-02-9 478737-04-1 478737-06-3 478737-08-5 478737-10-9 478737-12-1, **Apolipoprotein** L-3 (human gene APOL3) 478737-16-5 478737-18-7 478737-20-1 478737-23-4 478737-25-6, Gremlin (human gene CKTSF1B1) 478737-27-8, Chloride channel (human gene CLIC4) 478737-29-0 478737-31-4 478737-33-6 478737-35-8, Coatomer (human gene COPA subunit .alpha.) 478737-37-0 478737-39-2 478737-41-6 478737-43-8, Ephrin-A1 (human gene EFNA1) 478737-45-0, Epiplakin 1 (human gene EPPK1) 478737-47-2, Protein (human gene FLJ11350) 478737-49-4, Protein (human gene FLJ13809) 478737-51-8, Protein (human gene FLJ20500) 478737-53-0, Protein (human gene FLJ23399) **478737-55-2**, Fibronectin 1 (human gene FN1 isoform 1) **478737-57-4**, Fibronectin 1 (human gene FN1 isoform 2) 478737-59-6 478737-62-1 478737-64-3 478737-66-5, Chemokine I-TAC (human gene G1P3) 478737-68-7, Protein GW112 (human) 478737-70-1 478737-72-3 478737-74-5 478737-76-7 478737-78-9 478737-80-3 478737-82-5 478737-84-7 478737-86-9, Interleukin 8 (human gene IL8RA) 478737-88-1, Inhibin (human gene INHBA .beta.-subunit) 478737-90-5, Integrin .alpha.3 (human gene ITGA3 isoform a) 478737-92-7, Integrin .alpha.3 (human gene ITGA3 isoform b) 478737-94-9, Integrin .beta.6 (human gene ITGB6) 478737-96-1 478737-98-3 478738-00-0 478738-02-2 478738-04-4, Protein KIAA0662 (human) 478738-06-6, Laminin 5 (human gene LAMA3) 478738-08-8, Laminin .gamma.2 (human gene LAMC2) 478738-10-2 478738-12-4, Lumican (human gene LUM) 478738-14-6 478738-16-8 478738-19-1 478738-21-5, Midkine (human gene MDK) 478738-23-7 478738-25-9, Elastase (human gene MMP12) 478738-27-1, Stromelysin 1 (human gene MMP3) 478738-29-3, Matrilysin (human gene MMP7 isoenzyme 1)

478738-32-8, Gelatinase B (human gene MMP7) 478738-34-0, Mesothelin (human gene MSLN isoform 1) 478738-36-2, Mesothelin (human gene MSLN isoform 2) 478738-38-4, Mesothelin (human gene MSLN isoform 3) 478738-40-8, Mesothelin (human gene MSLN isoform 4) 478738-42-0, Mesothelin (human gene MSLN isoform 5) 478738-44-2, Mesothelin (human gene MSLN isoform 6) 478738-47-5, Episialin (human gene MUC1 isoform 2) 478738-49-7 478738-51-1 478738-53-3 478738-55-5 478738-57-7 478738-59-9 478738-61-3, Osteopontin (human gene OPN-a) 478738-63-5, Osteopontin (human gene OPN-b) 478738-65-7, Osteopontin (human gene OPN-c) 478738-67-9, Periostin (human gene OSF-2 isoform 1) 478738-69-1, Periostin (human gene OSF-2 isoform 2) 478738-71-5, Protein (human gene PIM-2) 478738-73-7 478738-75-9 478738-77-1, Pinin (human gene PNN) 478738-79-3, Proteoglycan 1 (human gene PRG1) 478738-81-7 478738-83-9, Pleiotrophin (human gene PTN) 478738-85-1 478738-87-3 478738-89-5 478738-91-9 478738-93-1 478738-95-3 478738-97-5 478739-00-3 478739-02-5 478739-04-7, Proteinase, TMPRSS4 (human) 478739-06-9, Thymosin .beta.4 (human gene TMSB4X) 478739-08-1 478739-10-5, Tropomyosin 1 (human gene TPM1) 478739-13-8 478739-15-0, Diubiquitin (human gene UBD) 478739-17-2 478739-19-4 478739-21-8 478739-23-0 478739-24-1, Osteonectin (human gene SPARC) 478739-25-2, Aquaporin 5 (human gene AQP5) 478739-26-3, Protein (human gene CDC20) 478739-28-5, Claudin-1 (human gene CLDN1) 478739-30-9, Protein (human gene MCM6) 478739-31-0, Episialin (human gene MUC1 isoform 1) 478739-33-2, Thioredoxin (human gene TXN)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; differentially expressed human genes and their encoded proteins useful for identification, assessment, prevention, and therapy of cervical cancer)

L16 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:906285 CAPLUS
DN 138:12035
TI Human cDNAs and proteins and their uses for screening and diagnostic assays
IN Bejanin, Stephane; Tanaka, Hiroaki
PA Genset, Fr.
SO PCT Int. Appl., 505 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002094864	A2	20021128	WO 2001-IB1715	20010806
	WO 2002094864	A3	20030619		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003027248	A1	20030206	US 2001-924340	20010806
	US 2003027161	A1	20030206	US 2001-992600	20011113
	US 2003157485	A1	20030821	US 2001-992095	20011113
	US 2003092011	A1	20030515	US 2001-489	20011114
	US 2003096247	A1	20030522	US 2001-986	20011114
	US 2003170628	A1	20030911	US 2001-999570	20011114
	US 2003198954	A1	20031023	US 2001-1142	20011114
	US 2003162186	A1	20030828	US 2002-154678	20020522
PRAI	US 2001-293574P	P	20010525		

US 2001-298698P P 20010615
US 2001-302277P P 20010629
US 2001-305456P P 20010713
US 2001-924340 A3 20010806
WO 2001-IB1715 W 20010806

IT **Apolipoproteins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(H; human cDNAs and proteins and their uses for screening and diagnostic assays)

IT 477744-37-9P 477744-39-1P 477744-41-5P 477744-43-7P 477744-45-9P
477744-50-6P 477744-52-8P 477744-54-0P 477744-56-2P 477744-58-4P
477744-60-8P 477744-62-0P 477744-64-2P 477744-66-4P 477744-68-6P
477744-70-0P 477744-72-2P 477744-74-4P 477744-76-6P 477744-78-8P
477744-80-2P 477744-82-4P 477744-84-6P 477744-86-8P 477744-88-0P
477744-90-4P 477744-92-6P **477744-94-8P** 477744-96-0P
477744-98-2P 477745-00-9P 477745-02-1P 477745-04-3P 477745-06-5P
477745-08-7P 477745-10-1P 477745-12-3P 477745-14-5P 477745-16-7P
477745-19-0P 477745-21-4P 477745-23-6P 477745-25-8P 477745-27-0P
477745-29-2P 477745-31-6P 477745-33-8P 477745-35-0P 477745-37-2P
477745-39-4P 477745-41-8P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; human cDNAs and proteins and their uses for screening and diagnostic assays)

L16 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:869083 CAPLUS
DN 137:381501
TI Protein-protein interaction domains of adipocyte proteins and method for screening for association-inhibiting drugs
IN Legrain, Pierre; Whiteside, Simon; Mao, Jen-I.; Khrebtukova, Irina; Luo, Shujun
PA Hybrigenics, Fr.; Lynx Therapeutics, Inc.
SO PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002090544	A2	20021114	WO 2002-EP6333	20020503
	WO 2002090544	A3	20031120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2003232421	A1	20031218	US 2002-139794	20020506
PRAI	US 2001-288885P	P	20010504		

IT Proteins
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ARP-1 (**apolipoprotein** A1 regulatory protein 1); protein-protein interaction domains of adipocyte proteins and method for screening for assocn.-inhibiting drugs)

IT 475603-56-6 475612-39-6 475612-40-9 475612-41-0 475617-37-9
475617-38-0 475617-39-1 475617-40-4 475617-41-5 475617-42-6
475617-43-7 475617-44-8 475617-45-9 475617-46-0 475617-47-1
475617-48-2 475617-49-3 475617-50-6 475617-51-7 475617-52-8
475617-53-9 475617-54-0 475617-55-1 475617-56-2 475617-57-3
475617-58-4 475617-59-5 475617-60-8 475617-61-9 475617-62-0
475617-63-1 475617-64-2 475617-65-3 475617-66-4 475617-67-5
475617-68-6 475617-69-7 475617-70-0 475617-71-1 475617-72-2
475617-73-3 475617-74-4 475617-75-5 475617-76-6 475617-77-7
475617-78-8 475617-79-9 475617-80-2 475617-81-3 475617-82-4
475617-83-5 475617-84-6 **475617-85-7** 475617-86-8
475617-87-9 475617-88-0 475617-89-1 475617-90-4 475617-91-5
475617-92-6 475617-93-7 475617-94-8 475617-95-9 475617-96-0
475617-97-1 475617-98-2 475617-99-3 475618-00-9 475618-01-0
475618-02-1 475618-03-2 475618-04-3 475618-05-4 475618-06-5
475618-07-6 475618-08-7 475618-09-8 475618-10-1 475618-11-2
475618-12-3 475618-13-4 475618-14-5 475618-15-6 475618-16-7
475618-17-8 475618-18-9 475618-19-0 475618-20-3 475618-21-4
475618-22-5 475618-23-6 475618-24-7 475618-25-8 475618-26-9
475618-27-0 475618-28-1 475618-29-2 475618-30-5 475618-31-6
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475618-42-9 475618-43-0 475618-44-1 475618-45-2 475618-46-3
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475618-52-1 475618-53-2 475618-54-3 475618-55-4 475618-56-5
475618-57-6 475618-58-7 **475618-59-8** 475618-60-1
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475618-66-7 475618-67-8 475618-68-9 475618-69-0 475618-70-3
475618-71-4 475618-72-5 475618-73-6 475618-74-7 475618-75-8
475618-76-9 475618-77-0 475618-78-1 475618-79-2 475618-80-5
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475619-15-9 475619-16-0 475619-17-1 475619-18-2 475619-19-3
475619-20-6 475619-21-7 475619-22-8 475619-23-9 475619-24-0
475619-25-1 475619-26-2 475619-27-3 475619-28-4 475619-29-5
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475619-35-3 475619-36-4 475619-37-5 475619-38-6 475619-39-7
475619-40-0 475619-41-1 475619-42-2 475619-43-3 475619-44-4
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475619-65-9 475619-66-0
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; protein-protein interaction domains of adipocyte proteins and method for screening for assocn.-inhibiting drugs)
IT 475619-67-1 475619-68-2 475619-69-3 475619-70-6 475619-71-7
475619-72-8 475619-73-9 475619-74-0 475619-75-1 475619-76-2
475619-77-3 475619-78-4 475619-79-5 475619-80-8 475619-81-9
475619-82-0 475619-83-1 475619-84-2 475619-85-3 475619-86-4
475619-87-5 475619-88-6 475619-89-7 475619-90-0 475619-91-1
475619-92-2 475619-93-3 475619-94-4 475619-95-5 **475619-96-6**
475619-97-7 475619-98-8 475619-99-9 475620-00-9 475620-01-0
475620-02-1 475620-03-2 475620-04-3 475620-05-4 475620-06-5
475620-07-6 475620-08-7 475620-09-8 475620-10-1 475620-11-2
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475620-22-5 475620-23-6 475620-24-7 475620-25-8 475620-26-9
475620-27-0 475620-28-1 475620-29-2 475620-30-5 475620-31-6
475620-32-7 475620-33-8 475620-34-9 475620-35-0 475620-36-1
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475620-46-3 475620-47-4 475620-48-5 475620-49-6 475620-50-9
475620-51-0 475620-52-1 475620-53-2 475620-54-3 475620-55-4
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475620-61-2 475620-62-3 475620-63-4 475620-64-5 475620-65-6
475620-66-7 475620-67-8 475620-68-9 475620-69-0 475620-70-3
475620-71-4 475620-72-5 475620-73-6 475620-74-7 475620-75-8
475620-76-9 475620-77-0 475620-78-1 **475620-79-2**
475620-80-5 475620-81-6 475620-82-7 475620-83-8 475620-84-9
475620-85-0 475620-86-1 475873-65-5 475873-66-6 475873-67-7
475873-68-8 475873-69-9 475873-70-2 475873-71-3 475873-72-4
475873-73-5 475873-74-6
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; protein-protein interaction domains of adipocyte proteins and method for screening for assocn.-inhibiting drugs)

L16 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:368513 CAPLUS
DN 136:380110
TI **Apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease
IN Graversen, Jonas; Moestrup, Soren
PA Proteopharma Aps, Den.
SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002038609	A2	20020516	WO 2001-DK739	20011109
	WO 2002038609	A3	20020926		
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002013843	A5	20020521	AU 2002-13843	20011109
	BR 2001015257	A	20030812	BR 2001-15257	20011109
	EP 1335938	A2	20030820	EP 2001-982197	20011109
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2002156007	A1	20021024	US 2001-987107	20011113
	NO 2003002101	A	20030708	NO 2003-2101	20030509
PRAI	DK 2000-1682	A	20001110		
	DK 2001-57	A	20010115		
	US 2001-264022P	P	20010126		
	WO 2001-DK739	W	20011109		

TI **Apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease
AB The invention relates to an **apolipoprotein** construct, an

apolipoprotein construct for use as a medicament, a nucleic acid sequence encoding the **apolipoprotein** construct, a vector comprising the nucleic acid sequence, a method for producing the **apolipoprotein** construct, and use of the **apolipoprotein** construct for the prepn. of apharmaceutical compn. Specifically, analogs and fusion proteins of **apolipoprotein** AI are described. The presented data document that the constructs according to the invention are capable of binding lipids, are capable of binding cubilin, which is a strong Apo AI receptor, stronger than native Apo A-I and that the plasma half life of the constructs is at least tripled compared to native Apo A-I. Together these data document that the constructs according to the invention are strong candidates for treatment of cardiovascular diseases.

ST **apolipoprotein** A analog fusion protein cardiovascular disease sequence; lipoprotein receptor binding **apolipoprotein** A analog fusion protein

IT **Apolipoproteins**
RL: DMA (Drug mechanism of action); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, analogs, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT **Apolipoproteins**
RL: DMA (Drug mechanism of action); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A-I, analogs, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT **Apolipoproteins**
RL: DMA (Drug mechanism of action); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A-II, analogs, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT **Apolipoproteins**
RL: DMA (Drug mechanism of action); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A-IV, analogs, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Transport proteins
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ABC (ATP-binding cassette) transporters, ABC1, **apolipoprotein** analogs binding; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Agglutinins and Lectins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(C-type (calcium-dependent type), oligomerization domain derived from; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT **Apolipoproteins**
RL: DMA (Drug mechanism of action); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E, analogs, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Immunoglobulins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(G3, linker peptide derived from hinge region of; **apolipoprotein** A analogs capable of forming HDL and with

extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Scavenger receptors
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SR-B1, **apolipoprotein** analogs binding; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Heart, disease
(angina pectoris, treatment and prevention of; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Heart, disease
(angina pectoris, unstable, treatment and prevention of; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Cardiovascular system, disease
Molecular association
(**apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Disulfide group
(**apolipoprotein** conjugates bonded via; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Proteins
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cholesterol ester-exchanging, **apolipoprotein** analogs binding; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Proteins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(collectins, fusion proteins contg. trimerization domain of; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Carbohydrates, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(conjugates with **apolipoprotein** derivs.; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Toxins
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(endotoxins, **apolipoprotein** derivs. for removal of; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Chimeric gene
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(for **apolipoprotein** A fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Albumins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(fragments, conjugates, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Immunoglobulins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(heavy chain, fragments, conjugates, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Lipoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-d.; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Heart, disease
(infarction, treatment and prevention of; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Receptors
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intrinsic factor; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Fibronectins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker peptide derived from; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker, in **apolipoprotein** A fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Pharmacokinetics
(of **apolipoprotein** A analogs; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Gene therapy
(of cardiovascular disease; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Proteins
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phospholipid-exchanging, **apolipoprotein** analogs binding; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Conformation
(protein, coiled-coil, in oligomerization of **apolipoprotein** derivs.; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Albumins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(serum, fragments, conjugates, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT Artery, disease
(stenosis, treatment and prevention of; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Liver
Macrophage
(therapeutic expression of **apolipoprotein** fusion protein gene in; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT Arteriosclerosis
(treatment and prevention of; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT **161238-68-2D**, fusion proteins
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(IgG3-derived linker peptide; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 426849-04-9 426849-05-0 426849-06-1 426849-07-2 426849-08-3 426849-09-4 426849-10-7 **426849-11-8 426849-12-9** 426849-15-2
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 426849-13-0D, 1-51-Tetranectin (human), substitution derivs., fusion products 426849-14-1D, Peptide Trip A (synthetic), substitution derivs., fusion products 426849-16-3D, 1-51-Tetranectin [50-serine] (human), substitution derivs., fusion products 426849-17-4D, 1-51-Tetranectin [50-threonine] (human), substitution derivs., fusion products 426849-18-5D, 1-51-Tetranectin [50-methionine] (human), substitution derivs., fusion products
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 426849-03-8D, fusion products
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT 18194-24-6, Dimyristoyl phosphatidylcholine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein** A analogs binding; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 37259-58-8D, Serine proteinase, fragments, conjugates, fusion proteins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 71-00-1D, L-Histidine, oligomers, fusion products 50812-37-8D, Glutathione-S-transferase, fusion products with **apolipoprotein** derivs.
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(**apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment

of cardiovascular disease)

IT 9031-14-5, Lecithin:cholesterol acyltransferase
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**apolipoprotein** analogs binding; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger receptor binding for treatment of cardiovascular disease)

IT **425371-33-1D**, fusion proteins 425371-34-2D, fusion proteins
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(fibronectin-derived linker peptide; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 9001-91-6, Plasminogen
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fragments, conjugates, fusion proteins; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 109489-77-2, Tetranectin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker peptide and oligomerization domain derived from; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT **425371-35-3D**, fusion proteins **425371-36-4D**, fusion proteins **425371-37-5D**, fusion proteins
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(synthetic linker peptide; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT **425371-32-0D**, fusion proteins
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(tetranectin-derived linker peptide; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 426869-71-8
RL: PRP (Properties)
(unclaimed protein sequence; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

IT 426869-72-9 426869-73-0 426869-74-1 426869-75-2 426869-76-3
426869-77-4 426869-78-5 426869-79-6 426869-80-9 426869-81-0
426869-82-1 426869-83-2 426869-84-3 426869-85-4 426869-86-5
426869-87-6 426869-88-7
RL: PRP (Properties)
(unclaimed sequence; **apolipoprotein** A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

L16 ANSWER 21 OF 22 USPATFULL on STN
AN 2002:280562 USPATFULL
TI **Apolipoprotein** analogues
IN Graversen, Jonas, Abyhoj, DENMARK
Moestrup, Soren, Aarhus, DENMARK
PA ProteoPharma ApS, Aarhus C, DENMARK (non-U.S. corporation)
PI US 2002156007 A1 20021024
AI US 2001-987107 A1 20011113 (9)
PRAI DK 2000-1682 20001110
DK 2001-57 20010115
US 2001-264022P 20010126 (60)

DT Utility
FS APPLICATION
LREP BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, WASHINGTON, DC, 20001-5303
CLMN Number of Claims: 84
ECL Exemplary Claim: 1
DRWN 23 Drawing Page(s)
LN.CNT 5048
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI **Apolipoprotein** analogues
AB The invention relates to a pharmaceutical composition comprising an **apolipoprotein** construct, to an **apolipoprotein** construct, a nucleic acid sequence encoding the **apolipoprotein** construct, a vector comprising the nucleic acid sequence, a method for producing the **apolipoprotein** construct, and a method of treatment comprising administering the **apolipoprotein** construct. The presented data document that the constructs according to the invention are capable of binding lipids, are capable of binding cubilin, which is a strong Apo Al receptor, stronger than native Apo A-I and that the plasma half life of the constructs is at least tripled compared to native Apo A-I. Together these data document that the constructs according to the invention are strong candidates for treatment of cardiovascular diseases.
PARN [0001] The invention relates to a pharmaceutical composition comprising an **apolipoprotein** construct, to an **apolipoprotein** construct, a nucleic acid sequence encoding the **apolipoprotein** construct, a vector comprising the nucleic acid sequence, a method for producing the **apolipoprotein** construct, and a method of treatment comprising administering the **apolipoprotein** construct.
SUMM [0002] In the following, the term Apo A or **apolipoprotein** A will be used to designate any of the three **apolipoproteins**, **Apolipoprotein** AI, **Apolipoprotein** AII, or **Apolipoprotein** AIV.

SUMM [0004] **Apolipoprotein** A-1 (apo-A-1) is the main component of plasma HDL (high density lipoprotein), which is negatively correlated to the presence of arterosclerosis. There is strong experimental evidence that this effect is caused by so-called reverse cholesterol transport from peripheral tissues to the liver. There is also experimental evidence that this reverse cholesterol transport can be stimulated in mammals by injection of apo-A-1.

SUMM [0005] **Apolipoprotein** A-1 is rapidly cleared from plasma. It is believed that Apo-A-1 is to a large extent removed from plasma by filtration in the kidneys without being broken down first (Braschi et al 1999, J Lipid Res, 40:522-532; Braschi et al 2000, Biochemistry, 39:5441-5449; Glass et al 1983, J Biol Chem 258:7161-7167). The short plasma half-life of **apolipoprotein** A is a constraint against using the protein in the treatment of atherosclerosis.

SUMM [0006] U.S. Pat. No. 5,876,968 (SIRTORI ET AL.) concerns substantially pure dimers of a variant of apo-A-1 called **apolipoprotein** A-1-Milano. Medicaments containing the dimer can be used for preventing thrombosis or they can be used as a prodrug for the monomer.

SUMM [0008] U.S. Pat. No. 5,643,757 (SHA-IL ET AL.) discloses a method for the production of pure, stable, mature and biologically active human **apolipoprotein** A-I in high yield.

SUMM [0009] U.S. Pat. No. 5,990,081 (AGELAND ET AL.) discloses a method for treatment of arterosclerosis or cardiovascular diseases by administering a therapeutically effective amount of apoliproprotein A or **apolipoprotein** E.

SUMM [0010] WO 96/37608 (RHONE-POULENC ROHRER ET AL.) describes human homologous dimers of **apolipoprotein** A-I variants comprising cystein in position 151. The presence of the cystein residue in the amino acid sequence allows the formation of dimers via disulphide bridges between the monomers. The reference furthermore discloses the corresponding nucleic acid sequences and vectors comprising these as well as pharmaceutical compositions comprising the variants and the use of these in gene therapy.

SUMM [0013] In a first aspect the invention relates to a pharmaceutical composition comprising an **apolipoprotein** construct having the general formula

SUMM [0015] where apo A is an **apolipoprotein** A component selected from the group consisting of **apolipoprotein** AI, **apolipoprotein** AII, **apolipoprotein** AIV, an analogue or a variant thereof,

SUMM [0017] with the proviso that when the construct consists of exactly two identical, native **apolipoproteins** these are linked serially.

SUMM [0018] By the invention is provided a novel pharmaceutical composition. The prior art fails to teach an apoliprotein construct as defined in the present invention for inclusion in a pharmaceutical composition. The **apolipoprotein** constructs according to the present invention may broadly be looked upon as HDL analogues due to their ability to form complexes with cholesterol and other lipids and assist in the transportation of these compounds to the liver.

SUMM [0019] Throughout the invention the **apolipoprotein** component or part of the construct is referred to as apo A or **apolipoprotein**. In the following and in the claims, the heterologous moiety is referred to as component X of the construct. The **apolipoprotein** or analogue or variant thereof is linked covalently to the heterologous moiety.

SUMM [0020] The component X of the construct may be looked broadly upon as a heterologous moiety. In this context a heterologous moiety is any kind of moiety not being linked to **apolipoprotein** or analogue or variant or functional equivalent thereof under native conditions. The heterologous moiety may thus be a peptide or a protein or part of a peptide or protein from the same or from another species, or even a single amino acid. It may be a synthetic peptide. It may be of carbohydrate nature or of other polymeric and biocompatible nature such as polyols, nucleic acids sequences.

SUMM [0021] Functional equivalence to native **apolipoprotein** A-I, A-II or A-IV may conveniently be measured using a lipid binding assay. The ability of the construct to elicit substantially the same physiological response in a mammal may conveniently be measured by measurement of the ability to perform reverse cholesterol transport in a test organism such as rabbits or rodent such as mice.

SUMM [0022] The construct comprising **apolipoprotein** and a heterologous moiety is capable of performing reverse cholesterol transport as well as or even better than native **apolipoproteins** , despite the modification caused by the addition of a heterologous moiety. The plasma half-life of the construct is preferably increased compared to that of the wild-type **apolipoprotein**. The increased half-life can be due either to the increased size of the **apolipoprotein** construct, which may reduce the rate of filtration through the kidneys, it may be due to increased binding to HDL, or it may be due to reduced breakdown of the construct compared to

native Apo A.

SUMM [0023] Preferably the plasma half-life is at least doubled or tripled, or at least quadrupled, or at least 10 doubled. Similarly, the binding affinity such as the lipid binding affinity, and/or the cholesterol binding affinity of the construct is preferably increased as compared to wild-type **apolipoprotein**. Preferably, the lipid binding affinity is increased by at least 5%, such as at least 10%, for example at least 15%, such as at least 20%, for example at least 25%, such as at least 30%, for example at least 40% such as at least 50%, for example at least 75%, such as at least 100%, such as at least 150%, for example at least 200%, such as at least 300%. Even in the cases where the lipid binding affinity of the constructs according to the invention is the same or lower than the lipid binding affinity of native **apolipoprotein**, the clinical effect may be enhanced due to increased plasma half life of the constructs according to the invention.

SUMM [0024] An increased plasma half-time and/or increased lipid binding affinity have profound implications for the use of the **apolipoprotein** constructs in the treatment of arterosclerosis. It is therefore expected that the clinical effect of the **apolipoprotein** constructs according to the invention is superior to the effect of wild-type **apolipoproteins**.

SUMM [0027] According to a second aspect of the invention, there is provided an **apolipoprotein** construct having the general formula

SUMM [0029] where apo A is an **apolipoprotein** component selected from the group consisting of **apolipoprotein** AI, **apolipoprotein** AII, **apolipoprotein** AIV, an analogue or a variant thereof,

SUMM [0030] and X is a heterologous moiety selected from the group consisting of an oligomerising module, and a terminally linked **apolipoprotein**.

SUMM [0031] According to a further aspect, there is provided a nucleotide sequence encoding an **apolipoprotein** construct as defined above. Preferably the nucleotide sequence is operably linked to a regulatory sequence for expression of the protein construct.

SUMM [0032] According to further aspects of the invention, there is provided a vector comprising the nucleotide sequence encoding the **apolipoprotein** construct and a transformed host cell comprising the nucleotide sequence as defined above.

SUMM [0033] The **apolipoprotein** construct according to the invention may be produced by different methods.

SUMM [0036] According to a second method the **apolipoprotein** construct can be manufactured by chemically synthesising the heterologous moiety and subsequently linking it to the **apolipoprotein** or analogue obtaining an **apolipoprotein** construct, which is isolated and optionally processed further. This method is the preferred method, when the heterologous moiety is of non-peptide nature. However there may also be conditions under which it is preferred to synthesise the heterologous moiety chemically, when it is of polypeptide nature. Such conditions may be that the heterologous moiety is rather short such as below 20 amino acids.

SUMM [0037] According to a third method the **apolipoprotein** construct can be manufactured by culturing a transformed host cell under conditions promoting the expression of an **apolipoprotein** or an **apolipoprotein** analogue encoded by a nucleic acid fragment and

subsequently covalently linking the **apolipoprotein** or **apolipoprotein** analogue to a heterologous moiety obtaining an **apolipoprotein** construct, isolating the resulting **apolipoprotein** construct and optionally further processing the construct.

SUMM [0038] Finally, the **apolipoprotein** construct may be produced by culturing a transformed host cell under conditions promoting the expression of a protein encoded by a nucleic acid fragment encoding an oligomerising module and subsequently linking said module to at least one **apolipoprotein** obtaining an **apolipoprotein** construct.

SUMM [0041] The **apolipoprotein** construct as defined above may also be used for gene therapy, wherein the DNA sequence encoding the **apolipoprotein** construct is used for transfection or infection of at least one cell population.

DRWD [0043] FIG. 1 shows the amino acid sequence (in one letter code) of human **apolipoprotein** A-I.

DRWD [0044] FIG. 2A shows CLUSTAL W (1.74) multiple sequence alignment of **apolipoprotein** A-I using BLOSUM. The following sequences are aligned in the Figure:

DRWD [0045] HUMAN sp|P026471|APA1_HUMAN **Apolipoprotein** A-I precursor (Apo-AI)--Homo sapiens (Human) Macaque sp|P15568|APA1_MACFA **Apolipoprotein** A-I precursor (Apo-AI)--Macaca fascicularis (Crab eating macaque) Bovine sp|P15497|APA1_BOVIN **Apolipoprotein** A-I precursor (Apo-AI)--Bos taurus (Bovine). Pig sp|P18648|APA1_PIG **Apolipoprotein** A-I precursor (Apo-AI)--Sus scrofa (Pig). Dog sp|P02648|APA1_CANFA **Apolipoprotein** A-I precursor (Apo-AI)--Canis familiaris (Dog). Rabbit sp|P09809|APA1_RABIT **Apolipoprotein** A-I precursor (Apo-AI)--Oryctolagus cuniculus (Rabbit).

DRWD [0046] Tree shreew sp|O18759|APA1_TUPGB **Apolipoprotein** A-I precursor (Apo-AI)--Tupaia glis belangeri (Common tree shrew).

DRWD [0047] Mouse sp|Q00623|APA1_MOUSE **Apolipoprotein** A-I precursor (Apo-AI)--Mus musculus (Mouse).

DRWD [0048] Rat sp|P04639|APA1_RAT **Apolipoprotein** A-I precursor (Apo-AI)--Rattus norvegicus (Rat). Eur. Hedgehog tr|Q9TS49 **APOLIPOPROTEIN** A-I, APOA-I=CHOLESTEROL TRANSPORTER--Erinaceus europaeus (Western European hedgehog).

DRWD [0049] Chicken sp|P08250|APA1_CHICK **Apolipoprotein** A-I precursor (Apo-AI)--Gallus gallus (Chicken).

DRWD [0050] Jap. quail sp|P329181|APA1_COTJA **Apolipoprotein** A-I precursor (Apo-AI)--Coturnix coturnix japonica (Japanese quail).

DRWD [0051] Domestic duck sp|O42296|APA1ANAPL **Apolipoprotein** A-I precursor (Apo-AI)--Anas platyrhynchos (Domestic duck).

DRWD [0052] Rainbow trout sp|O57523|AP11_ONCMY **Apolipoprotein** A-I-1 precursor (APOA-I-1)--Oncorhynchus mykiss (Rainbow trout) (Salmo gairdneri).

DRWD [0053] Brown trout sp|Q91488|APA1_SALTR **Apolipoprotein** A-I precursor (Apo-AI)--Salmo trutta (Brown trout).

DRWD [0054] Atl. salmon sp|P27007|APA1_SALSA **Apolipoprotein** A-I precursor (Apo-AI)--Salmo salar (Atlantic salmon).

DRWD [0055] Zebrafish sp|O42363|APA1_BRARE **Apolipoprotein** A-I precursor (Apo-AI)--Brachydanio rerio (Zebrafish) (Zebra danio).

DRWD [0056] Sea bream sp|O42175|APA1_SPAAU **Apolipoprotein** A-I precursor (Apo-AI)--Sparus aurata (Gilthead sea bream).

DRWD [0057] FIG. 2B shows aligned amino acid sequences (in one letter code) for human, macaque, mouse, baboon, pig, and rat **apolipoprotein** A-IV. FIG. 3: Amino acid sequence of the amino terminal region of tetranectin (SEQ ID NO 12). Amino acid sequence (in one letter code) from EI to L51 of tetranectin. Exon 1 comprises residues EI to D16 and exon 2 residues V17 to V49, respectively. The alpha helix extends beyond

L51 to K52 which is the C-terminal amino acid residue in the alpha helix.

DRWD [0064] FIG. 10 A to G shows illustrative examples of plasmids and corresponding amino acid sequences for **apolipoprotein** constructs according to the present invention.

DRWD [0076] FIG. 14 shows the results of the evaluation of plasma clearance of **apolipoprotein** A-I, TripA Apo-AI, and TripA-fibronectin-linker Apo A-I in mice. Experimental details can be found in Example 8.

DETD [0078] The **Apolipoprotein** or Analogue

DETD [0079] In the following the term "apo-A" is used to designate any **apolipoprotein** A comprising **apolipoprotein** A-I, **apolipoprotein** A-II or **apolipoprotein** A-IV, any variant or analogue thereof possessing the same lipid binding function.

DETD [0080] Preferred **apolipoprotein** A-I analogues include those disclosed in FIG. 2A. Preferred **apolipoprotein** A-IV analogues include those disclosed in FIG. 2B.

DETD [0082] According to the invention the term "**apolipoprotein**" is meant to include functional equivalents of at least one sequence in FIG. 1, 2a and 2b, or a fragment of at least one sequence in FIG. 1, 2a and 2b, comprising a predetermined amino acid sequence. A "fragment" is defined as:

DETD [0085] According to the present invention a functional equivalent of an **apolipoprotein** or fragments thereof may be obtained by addition, substitution or deletion of at least one amino acid. When the amino acid sequence comprises a substitution of one amino acid for another, such a substitution may be a conservative amino acid substitution. Fragments of the sequences in FIG. 1, 2a and 2b may comprise more than one such substitution, such as e.g. two conservative amino acid substitutions, for example three or four conservative amino acid substitutions, such as five or six conservative amino acid substitutions, for example seven or eight conservative amino acid substitutions, such as from 10 to 15 conservative amino acid substitutions, for example from 15 to 25 conservative amino acid substitution, such as from 25 to 75 conservative amino acid substitutions, for example from 75 to 125 conservative amino acid substitutions, such as from 125 to 175 conservative amino acid substitutions. Substitutions can be made within any one or more groups of predetermined amino acids.

DETD [0089] The addition or deletion of an amino acid may be an addition or deletion of from 2 to 10 amino acids, such as from 10 to 20 amino acids, for example from 20 to 30 amino acids, such as from 40 to 50 amino acids. However, additions or deletions of more than 50 amino acids, such as additions from 10 to 200 amino acids, are also comprised within the present invention. More specifically, 43 N-terminal amino acids may be removed from the sequence in FIG. 1 without substantially altering the lipid binding effect of the protein. Such a deletion variant is included in SEQ ID NO 4 as the **apolipoprotein** part of the construct.

DETD [0090] It will thus be understood that the invention concerns **apolipoproteins** comprising at least one fragment of the sequences in FIG. 1, 2a or 2b capable of binding lipids such as DPMC, including any variants and functional equivalents of such at least one fragment.

DETD [0091] The **apolipoprotein** according to the present invention, including any functional equivalents and fragments thereof, may in one embodiment comprise less than 243 amino acid residues, such as less than 240 amino acid residues, for example less than 225 amino acid residues, such as less than 200 amino acid residues, for example less than 180 amino acid residues, such as less than 160 amino acid residues, for example less than 150 amino acid residues, such as less than 140 amino acid residues, for example less than 130 amino acid residues, such as less than 120 amino acid residues, for example less than 110 amino acid residues, such as less than 100 amino acid residues, for example less than 90 amino acid residues, such as less than 85 amino acid residues, for example less than 80 amino acid residues, such as less than 75 amino acid residues, for example less than 70 amino acid residues, such as

less than 65 amino acid residues, for example less than 60 amino acid residues, such as less than 55 amino acid residues, for example less than 50 amino acid residues.

DETD [0096] AII fragments or functional equivalents of **apolipoprotein** are included within the scope of this invention, regardless of the degree of homology that they show to a preferred predetermined sequence of **apolipoprotein**. The reason for this is that some regions of the sequences in FIG. 1, 2a or 2b are most likely readily mutatable, or capable of being completely deleted, without any significant effect on the binding activity of the resulting fragment.

DETD [0099] Fragments sharing at least some homology with the sequences in FIG. 1, 2a or 2b fragment are to be considered as falling within the scope of the present invention when they are at least about 40 percent homologous with the **apolipoprotein** or fragment thereof, such as at least about 50 percent homologous, for example at least about 60 percent homologous, such as at least about 70 percent homologous, for example at least about 75 percent homologous, such as at least about 80 percent homologous, for example at least about 85 percent homologous, such as at least about 90 percent homologous, for example at least 92 percent homologous, such as at least 94 percent homologous, for example at least 95 percent homologous, such as at least 96 percent homologous, for example at least 97 percent homologous, such as at least 98 percent homologous, for example at least 99 percent homologous with the sequences in FIG. 1, 2a or 2b fragment.

DETD [0102] Conservative substitutions may be introduced in any position of a preferred predetermined **apolipoprotein** or fragment thereof. It may however also be desirable to introduce non-conservative substitutions, particularly, but not limited to, a non-conservative substitution in any one or more positions.

DETD [0108] Preferably the component X is non inmmunogenic and does not interfere negatively with regard to ligand binding, i.e. the **apolipoprotein** component should not be directed at an undesired site through interactions of the X-component with a ligand.

DETD [0109] According to one embodiment the component X consists of just one amino acid, which amino acid preferably is a cystein residue, which may be placed N-terminally, C-terminally or internally in the **apolipoprotein** component. Such a construct may form a dimer with other identical or similar constructs. Preferably a linker is introduced between the terminal cystein residue and the **apolipoprotein** component to facilitate the correct folding and lipid interaction of the construct.

DETD [0111] In the case where the X-component is a protein, this protein is preferably a mammalian protein and more preferably a human protein. Examples of suitable proteins include plasma proteins such as albumin or serum albumin or another non-immunogenic peptide or protein such as the serine protease fragment of plasminogen or another serine protease engineered to be inactive by disruption of the catalytic triad; and the constant region of the heavy chain of immunoglobins. More preferably, the protein comprises serum albumin. Even more preferably the protein comprises an **apolipoprotein** containing an amphipatic helix containing **apolipoprotein**.

DETD [0112] According to an especially preferred embodiment of the invention, the component X comprises an **apolipoprotein** component selected from the group consisting of **apolipoprotein** A-I, A-II, AIV, an analogue, functional variant or fragment thereof. The two **apolipoprotein** components may be linked linearly or they may be linked via an additional non-native terminal cystein bridge.

DETD [0113] Higher oligomers as well as dimers of the **apolipoprotein** component comprising at least one non-native cystein residue may be manufactured and linked through cystein bridges under appropriate conditions. Oligomers linked by disulphide bridges may be linked serially (apo-A-S-S-apo-A, or apo-A-S-S-apo-A-S-S-apo-A or higher oligomers).

DETD [0114] The protein construct according to the invention may also

comprise two, three or more **apolipoproteins** or analogues thereof being serially and covalently linked to one another. This may be achieved by linking the C-terminal of a first **apolipoprotein** to the N-terminus of the next **apolipoprotein** and so forth. The proteins may be so linked after transcription and translation or the nucleotide sequence may simply comprise two, three or more sequences coding for the **apolipoprotein** construct in question as well as optional linker peptides between the **apolipoproteins**.

DETD [0116] Such constructs comprising more than one **apolipoprotein** component may comprise a combination selected from the following group:

Dimers:
A-I A-I; A-II AII; A-IV A-IV; A-I A-II; A-I A-IV; A-II A-IV.

Trimers:
A-I A-II A-IV; A-I A-I A-II; A-I A-I A-I; A-I A-I A-IV; A-II A-II A-I; A-II A-II A-IV; A-II A-II A-II; A-IV A-IV A-IV; A-IV A-IV A-II; A-IV A-IV A-I.

DETD [0120] When the **apolipoprotein** or analogue part of the construct is coupled to an oligomerising module, multimers of the construct can be made by simply mixing a solution of constructs (oligomerisation module linked to **apolipoprotein** part) under appropriate conditions. In this way, dimers, trimers, tretramers, pentamers, hexamers or higher -mers can be made depending on the type of oligomerising module being linked to the **apolipoprotein** part of the construct.

DETD [0121] The multimers according to the invention may be homomers or heteromers, since different **apolipoproteins** can be linked to the oligomerising modules and be incorporated into the multimer. It may be advantageous to mix the different types of **apolipoproteins** in this way to obtain an improved clinical effect of the construct. Preferred homomers include trimers of Apo-A-I and trimers of Apo-A-IV.

DETD [0128] According to a preferred embodiment of the invention the protein construct is obtained by linking two or more **apolipoproteins** to oligomerising modules. The advantage of this embodiment is that the linkage of the individual **apolipoproteins** to one another does not take place within the **apolipoprotein** but in the oligomerising module. Thereby the nature of the wild-type **apolipoprotein** is conserved and the **apolipoprotein** conserves the secondary and tertiary structure, which is advantageous for its physiological function. By further introducing a peptide spacer between the **apolipoprotein** and the oligomerising module it is ensured that both of the components of the construct can perform their interaction with lipids and other oligomerising modules respectively without being affected by the interactions of the other component. Preferably, the peptide spacer is non-immunogenic, and has an essentially linear three dimensional structure.

DETD [0130] The general method for producing an artificial trimer of a protein or peptide comprises the identification of a trimerisation module from proteins that form trimers in nature. Through careful analysis, the domain responsible for the protein-protein interaction can be identified, isolated, and linked to the protein or peptide to be trimerised. According to the invention such trimerisation does not necessarily comprise the formation of a trimer of **apolipoprotein** or an analogue. It is also possible to link just one **apolipoprotein** to a trimerisation module and allow this peptide to trimerise with two other trimerisation modules. Thereby the molecular weight of the **apolipoprotein** part is increased and the plama half-life may be increased compared to native **apolipoprotein**.

DETD [0132] Another example of an oligomerisation module is the .alpha.1-chain from Haptoglobin. The .alpha.1-chain has a cystein residue which may link to another .alpha.1-chain to form a dimer. A natural variant is the .alpha.2-chain, which has had part of the .alpha.1-chain involved in disulphide bridging duplicated. The

.alpha.2-chain may form cystein bridges to cystein residues in other .alpha.2 or .alpha.1-chains thereby forming trimers, tetramers, pentamers, hexamers and higher -mers. In the natural form the .alpha.-chain is associated to a .beta.-chain. It is possible to replace the .beta.-chain with an **apolipoprotein** to make an apo-A-.alpha.-chain (haptoglobin) construct.

DETD [0134] The protein construct may also advantageously comprise a spacer moiety, which is covalently linked between the **apolipoprotein** or **apolipoprotein** analogue and the heterologous moiety. The effect of the spacer is to provide space between the heterologous moiety and the **apolipoprotein** part of the construct. Thereby is ensured that the secondary structure of the **apolipoprotein** part is not affected by the presence of the heterologous moiety so that the physiological effect of the **apolipoprotein** part is maintained. Preferably, the spacer is of polypeptide nature. In this way the nucleic acid sequence encoding the spacer can be linked to the sequence encoding the **apolipoprotein** part of the construct and optionally the sequence for the heterologous moiety, and the whole construct can be produced at the same time.

DETD [0136] A spacer moiety may also be inserted between two TTSEs allowing both of these to interact with a third separate TTSE to form a trimeric complex, which then comprises two separate peptides: TTSE and TTSE-spacer-TTSE. This embodiment facilitates the production of the **apolipoprotein** construct since the major part of the trimer, which is then strictly seen a dimer, can be synthesised as one single polypeptide comprising in the fusion partners (apo-A denoting any polypeptide sequence forming the **apolipoprotein** part of the construct) apo-A-TTSE-spacer-TTSE-apo-A.

DETD [0141] The following are examples of spacer sequences, which are believed to be especially preferable for linking **apolipoprotein** analogues to a component X. Preferred examples of spacer or linker peptides include those, which have been used to link proteins without substantially impairing the function of the linked proteins or at least without substantially impairing the function of one of the linked proteins. More preferably the linkers or spacers have been used to link proteins comprising coiled-coil structures.

DETD [0155] One especially preferred embodiment of the invention is the trimerisation or partial trimerisation of an **apolipoprotein** or analogue thereof with the trimerisation module from tetranectin.

DETD [0198] The performance of the constructs according to the invention may be analysed by measuring the ability of the constructs to bind to receptors or HDL proteins which may bind native **apolipoprotein** A-I, A-II or A-IV. Such receptors and proteins include but are not limited to cubilin, megalin, Scavenger receptor class B type 1 (SR-B1), ATP-binding cassette 1 (ABC1), Lecithin:cholesterol acyltransferase (LCAT), Cholesteryl-ester transfer protein (CETP), Phospolipid transfer protein (PLTP). The dissociation constant, Kd, of the complex between cubilin and native **apolipoprotein** A I is 20 nM. It has been determined experimentally that an **apolipoprotein** A I trimer according to the present invention binds even stronger to cubilin (FIG. 12).

DETD [0205] In order to produce a construct comprising an **apolipoprotein** part and a TTSE, the cDNA encoding the **apolipoprotein** part is ligated at the 3' end to the 5' end of the c-DNA encoding the TTSE. Further TTSE units and **apolipoprotein** units may also be ligated. A sequence encoding an enzyme cleavage site is further ligated to the 3' end of the sequence encoding TTSE and finally a sequence encoding polyhistidine is also ligated. This can be done by conventional PCR techniques. The combined c-DNA is inserted into an expression vector and transformed into a host cell.

DETD [0212] The apo-A-constructs according to the invention may be administered for prevention and/or treatment of diseases related to cholesterol, phospholipids, and triacylglycerides, LDL and HDL disorders

such as hypercholesterolemia, and arteriosclerotic diseases such as atherosclerosis and myocardial infarct. Other indications include angina pectoris, plaque angina pectoris, unstable angina pectoris, arterial stenoses such as carotis stenosis, claudicatio, or cerebral arterial stenosis. Furthermore, the **apolipoprotein** constructs may be used for removal of endotoxins.

DETD [0213] In one embodiment, administration comprises the administration of at least 50 mg of the construct every week such as to obtain a plasma concentration of approximately 0.5 g/L. Preferably the construct is administered parenterally such as through injections, suppositories, implants etc. Preferably the composition is administered in an amount comprising at least 50 mg **apolipoprotein** construct per week, such as at least 100 mg/week, for example at least 250 mg/week, such as at least 500 mg/week, for example at least 750 mg/week such as at least 1000 mg/week, for example at least 1250 mg/week, such as at least 1500 mg/week, for example at least 2000 mg/week, such as at least 2500 mg/week, for example at least 5000 mg/week. The administration may be performed daily, every two or three days, once a week, once every second week, or once every third week, or once every fourth week.

DETD [0223] Expression of **Apolipoprotein** A-I (apo A-I) in E. coli Ubi-A-I and Trip-A-I as well as the other constructs disclosed in the figures are conveniently expressed in E. coil AV-1 cells (Stratagene Inc.). Other cell lines may be used as well. Culturing of the cells and induction of expression were performed as described for tetranectin in WO 98/56906.

DETD [0243] The assay was conducted as described in: Kozyraki R, Fyfe J, Kristiansen M, Gerdes C, Jacobsen C, Cui S et al. The intrinsic factor-vitamin B12 receptor, cubilin, is a high-affinity **apolipoprotein** A-I receptor facilitating endocytosis of high-density lipoprotein. Nat Med 1999; 5(6):656-661. The concentration of **apolipoprotein** construct used was 0.5 .mu.M. Results (FIG. 12) are only shown for TripA-AI and apo A-I. Binding similar to that observed for TripA-AI was observed for TripA-FN-AI and TripA-TN-AI. The response increased upon trimerisation of apo A-I, especially there was a decrease in the of-rate, based on the gained "avidity" of the interaction for a multimer with an immobilised target compared to a monomer (bonus of multivalency). Showing that apo A-I was able to bind cubilin in the trimeric state, and that more than one apo A-I was in a conformation capable of interacting with cubilin, indicating correct folding of the apo A-I unit in the trimeric construct.

DETD [0244] Evaluation of The Plasma Clearance of **Apolipoprotein** A-I, TripA Apo-A-I and TripA fibronectin-linker Apo-A-I in mice.

DETD [0246] The plasma concentrations of **apolipoprotein** A-I and derivatives were measured using an ELISA assay as follows:

DETD [0275] Finally the plasmid comprises the human apoliprotein A-I cDNA coding for amino acids 25-267 from human **apolipoprotein** A-I. The expressed and purified protein corresponds to SEQ ID NO 3.

DETD [0277] The plasmid comprises the sequences as above, but the **apolipoprotein** part has been replaced with cDNA coding for amino acids 68-267 from human **apolipoprotein** A-I. The expressed and purified protein corresponds to SEQ ID NO 4

DETD [0285] ApoAI: cDNA coding for amino acids 25-267 from human **apolipoprotein** A-I The expressed and purified protein corresponds to SEQ ID NO 1.

DETD [0287] As above, but after the sequence coding for the two glycine residues and before the **apolipoprotein** A-I sequence coding for a cystein residue has been inserted. The expressed and purified protein corresponds to SEQ ID NO 2.

DETD [0295] ApoAI: cDNA coding for amino acids 25-267 from human **apolipoprotein** A-I The expressed and purified protein corresponds to SEQ ID NO 2.

DETD [0296] Further examples of plasmids for expression of **apolipoprotein** constructs according to the invention are disclosed in FIG. 10A to G together with the corresponding amino acid

sequences of the expressed and purified proteins, which are disclosed in the sequence listing.

CLM What is claimed is:

1. A pharmaceutical composition comprising an **apolipoprotein** construct having the general formula apo-A-X, where apo-A is an **apolipoprotein** component selected from the group consisting of **apolipoprotein** AI, **apolipoprotein** AII, **apolipoprotein** AIV, a functional analogue or variant thereof, and X is a heterologous moiety comprising at least one compound selected from the group consisting of an amino acid, a peptide, a protein, a carbohydrate, and a nucleic acid sequence, with the proviso that when the construct consists of exactly two identical, native **apolipoproteins** these are linked serially.

11. The composition according to claim 7, wherein the protein comprises at least one amphipatic helix containing **apolipoprotein**.

12. The composition according to claim 1, wherein the component X comprises at least one **apolipoprotein** A-I, **apolipoprotein** A-II **apolipoprotein** A-IV, **Apolipoprotein** E, an analogue or variant thereof.

13. The composition of claim 12, wherein the analogue or variant is capable of eliciting substantially the same physiological response as the **apolipoprotein**-A-I A-II or A-IV.

25. The composition of the claim 21, wherein the trimerising module comprises two tetranectin trimerising modules linked by a spacer moiety, which allows both of the two tetranectin trimerising modules to take part in a complex formation with a third tetranectin trimerising module not being part of the **apolipoprotein** construct.

38. An **apolipoprotein** construct having the general formula apo-A-X, where apo-A is an **apolipoprotein** component selected from the group consisting of **apolipoprotein** AI, **apolipoprotein** AII, **apolipoprotein** AIV, an functional analogue or variant thereof, and X is a heterologous moiety selected from the group consisting of an oligomerising module, and a terminally linked **apolipoprotein**.

43. The construct according to claim 38, wherein component X comprises at least one amphipatic helix containing **apolipoprotein**.

44. The construct according to claim 38, wherein the **apolipoprotein** comprises at least one **apolipoprotein** A-I, **apolipoprotein** A-II, **apolipoprotein** A-IV, **Apolipoprotein** E, an analogue or variant thereof.

45. The construct of claim 44, wherein the analogue or variant is capable of eliciting substantially the same physiological response as the **apolipoprotein**-A-I, A-II or A-IV.

55. The construct of the claims 51, wherein the trimerising module comprising two tetranectin trimerising modules linked by a spacer moiety, which allows both of the two tetranectin trimerising modules to take part in a complex formation with a third tetranectin trimerising module not being part of the **apolipoprotein** construct.

63. Nucleic acid comprising a sequence of nucleotides encoding an **apolipoprotein** construct as defined in claim 1.

68. A method for the production of an **apolipoprotein** construct as defined in the claims 1, comprising the steps of: culturing a transformed host cell under conditions promoting the expression of a

protein construct according to claims 1, obtaining and recovering said protein construct, optionally, further processing said protein construct.

71. The method of claim 69, comprising administering to an individual a composition comprising at least 50 mg **apolipoprotein** construct per week, preferably at least at least 100 mg/week, for example at least 250 mg/week, such as at least 500 mg/week, for example at least 750 mg/week such as at least 1000 mg/week, for example at least 1250 mg/week, such as at least 1500 mg/week, for example at least 2000 mg/week, such as at least 2500 mg/week, for example at least 5000 mg/week.

IT **161238-68-2D**, fusion proteins
(IgG3-derived linker peptide; apolipoprotein A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)
IT 426849-04-9 426849-05-0 426849-06-1 426849-07-2 426849-08-3 426849-09-4 426849-10-7 **426849-11-8** **426849-12-9** 426849-15-2
(amino acid sequence; apolipoprotein A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)
IT **425371-33-1D**, fusion proteins 425371-34-2D, fusion proteins
(fibronectin-derived linker peptide; apolipoprotein A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)
IT **425371-35-3D**, fusion proteins **425371-36-4D**, fusion proteins **425371-37-5D**, fusion proteins
(synthetic linker peptide; apolipoprotein A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)
IT **425371-32-0D**, fusion proteins
(tetranectin-derived linker peptide; apolipoprotein A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease)

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AN 2001:763189 CAPLUS
DN 135:328141
TI Human gene Zmax1 of 11q13.3, HBM (high bone mass) allele, encoded polypeptides, and their diagnostic and therapeutic uses
IN Carulli, John P.; Little, Randall D.; Recker, Robert R.; Johnson, Mark L.
PA Genome Therapeutics Corporation, USA
SO PCT Int. Appl., 443 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001077327	A1	20011018	WO 2000-US16951	20000621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1268775	A1	20030102	EP 2000-941578	20000621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

US 2003219793 A1 20031127 US 2003-374979 20030228
PRAI US 2000-543771 A 20000405
US 2000-544398 A 20000405
US 2000-578900 W 20000526
WO 2000-US16951 W 20000621
US 2002-240851 A1 20021004
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT **Apolipoproteins**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E; human gene Zmax1 of 11q13.3, HBM (high bone mass) allele, encoded polypeptides, and their diagnostic and therapeutic uses)
IT 131143-45-8, .alpha.-Actinin (human clone p5.alpha.A subunit precursor reduced) 161414-74-0 161736-33-0 172493-32-2 185970-14-3 194244-12-7 200761-62-2 211626-03-8 212843-80-6 218619-98-8 219578-03-7 285578-73-6, Protein (human gene LIMD1) 369415-64-5, Protein (human gene AES) 369415-65-6, Ajuba (human) 369415-66-7, Protein (human gene HSM800944) 369415-67-8 369415-68-9, Protein (human gene DEEPEST) **369415-69-0**, Fibronectin (human gene FN) 369415-70-3, Glutamine-lysine-rich protein (human) 369415-71-4, Protein (human gene HOXB13) 369415-72-5, PINCH-like protein (human) 369415-73-6, Protein (human gene TCB) 369415-74-7, Protein (human gene TRIO)
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; human gene Zmax1 of 11q13.3, HBM (high bone mass) allele, encoded polypeptides, and their diagnostic and therapeutic uses)